Dissertation on

A STUDY ON PREVALENCE OF ELEVATED HOMOCYSTEINE LEVEL IN PATIENTS WITH STROKE IN YOUNG

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CERTIFICATE

This is to certify that the dissertation titled **"A STUDY ON PREVALENCE OF ELEVATED HOMOCYSTEINE IN PATIENTS WITH STROKE IN YOUNG "** submitted by **Dr. R.VIVEK PRAVEEN** appearing for Part II M.D Branch I General Medicine Degree examination in April 2011 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of the Tamilnadu Dr. M. G. R.Medical University, Chennai. I forward this to the Tamilnadu Dr. M.G. R. Medical University,

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DECLARATION

I, **Dr.R.VIVEK PRAVEEN** solemnly declare that this dissertation entitled **"A STUDY ON PREVALENCE OF ELEVATED HOMOCYSTEINE LEVEL IN PATIENTS WITH STROKE IN YOUNG"** is a bonafide work done by me at Madras Medical College and Government General Hospital from JANUARY 2009 to JUNE 2010 under the guidance and supervision of my unit chief **Prof.C.RAJENDIRAN, M.D.,** Director and Professor, Institute of Internal Medical, Madras Medical College, Chennai.

This dissertation is submitted to The Tamil Nadu Dr. M. G. R. Medical University, towards fulfillment of regulation for the award of M. D. degree (Branch- I) in General Medicine.

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CONTENTS

INTRODUCTION

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GLOBAL TRENDS IN STROKE

Stroke is a Non-communicable disease of increasing socioeconomic importance in ageing populations. According to WHO, stroke was the second commonest cause of worldwide mortality in 1990 and, the third commonest cause of mortality in more developed countries. it was responsible for about 4·4 million deaths worldwide. In the recent estimates made in 1999, the number of deaths due to stroke reached 5·54 million worldwide, with two-thirds of these deaths occurring in less developed countries. Stroke is also a major cause of long-term disability and, has potentially enormous emotional and socioeconomic consequences for patients, their families, and health services. The case-fatality rate due to stroke is reported to vary from 11.7% to 32.4%.

In 2005, estimates indicated that 58 million people died, and in them chronic diseases accounted for 35 million deaths (60%).

Cardiovascular diseases, predominantly heart disease and stroke, were the cause of death in 17·5 million individuals. After heart disease, Stroke is the second leading single cause of death, with 5·8 million fatal cases per year, 40% of which are in people younger than 70 years. About 15 million new acute stroke events arise every year, and about 55 million people have had a stroke at some time in the past, either with or without residual disability; two-thirds of these individuals live in low income and middle-income countries.

Demographic changes, urbanization, and increased exposure to major stroke risk factors will fuel the stroke burden in the future. By 2025, four out of five stroke events will occur in people living in these regions. The prevalence of stroke in India varies in different regions of the country and, ranges from 40 to 270 per 100 000 population. Approximately 12% of all strokes occur in the population <40 years of age. Major risk factors identified in India are hypertension (blood pressure >95 mm Hg diastolic), hyperglycemia, tobacco use, and low hemoglobin levels (<10 gm %). Stroke accounts for 2 percent of hospital registrations, 1.5 percent of medical registrations and 9 to 30 percent of neurological admissions in major hospitals.

The National Commission on Macroeconomics and Health has projected that cases of stroke would increase from 1,081,480 in 2000 to 1,667,372 in 2015.

BURDEN OF STROKE IN INDIA[2]

Year/Age (Years)	Estimated prevalence of stroke per 1000	Estimated population	Estimated cases
2000			
20 – 39	**0.3022**	**306,904,000**	**92,746**
40 – 59	**2.7188**	**168,223,000**	**457,365**
60 – 79	**8.4733**	**62,711,000**	**531,369**
Others		**464,304,000**	**----**
Total		**1,002,142,000**	**1,081,480**
2005			
20 – 39	**0.3022**	**346,437,000**	**104,693**
40 – 59	**2.7188**	**196,422,000**	**543,032**
60 – 79	**8.4733**	**71,883,000**	**609,086**
Others		**468,027,00**	**----**
Total		**1,082,769,000**	**1,247,812**
2010			
20 – 39	**0.3022**	**392,531,000**	**118,623**
40 – 59	**2.7188**	**227,674,000**	**619,000**
60 – 79	**8.4733**	**84,168,000**	**713,181**
Others		**463,688,000**	**----**
Total		**1,168,061,000**	**1,450,804**
2015			
20 – 39	**0.3022**	**428,582,000**	**129,517**
40 – 59	**2.7188**	**258,731,000**	**703,438**
60 – 79	**8.4733**	**98.476,000**	**834,417**
Others		**466,053,000**	**----**
Total		**1,251,842,000**	**1,667,372**

STUDIES ON STROKE DONE IN INDIA

	Place	Age Group	No.of Patients	Aim of the study
Nayak et al	**Trivandrum**	**15 – 45 Years**	**177**	**Clinical features and risk factors**
Lipska et al	**Trivandrum**	**15 – 45 years**	**214**	**Risk factors**
Razdan et al	**Rural Kashmir**	**>15 years, sub group 15 – 39, 40 – 49 years**	**91**	**Prevalence study**
Abraham et al	**Vellore**	**All age groups**	**147**	**Prevalence study**
Das et al	**Kolkata**	**All age groups, subgroup <40 years and >40 years**	**247**	**Prevalence and incidence study**
Dalal et al	**Mumbai**	**>25 years, subgroups 25 – 34 and 35 – 44 years**	**456**	**Incidence study**

STUDIES ON STROKE DONE OUTSIDE INDIA

	Place/Country	Age group (years)	No. of patients
Adams et al	**Lowa, USA**	**15 – 45**	**329**
Kittner et al	**Baltimore, USA**	**15 – 44**	**428**
You et al	**Melbourne, Australia**	**15 – 55**	**201**
Marini et al	**La Aquila**	**<45**	**89**
Jacobs et al	**Manhattan, NY, USA**	**20 – 44**	**74**
Lee et al	**Taiwan**	**18 – 45**	**264**
Leys et al	**France**	**15 – 45**	**287**
Kristensen et al	**Sweden**	**18 – 44**	**107**
Nedeltchev et al	**Switzerland**	**16 – 45**	**203**
Putaala et al	**Helsinki**	**15 – 49**	**1008**
Verona et al	**Spain**	**15 – 45**	**272**

AIMS AND OBJECTIVES

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1. To determine the prevalence of elevated homocysteine level in 50 patients with stroke in young .
2. To study about the role of homocysteine levels in predicting morbidity and mortality.
3. To study about prognostic implication of elevated homocysteine level.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

STROKE IN YOUNG

Stroke is a major public health problem. Stroke is also the most common neurological condition causing long-term disability and has enormous emotional and socioeconomic consequences in patients, their families and health services. The latest available estimates from Indian Council of Medical Research (ICMR) indicate that in 2004 there were 930,985 cases of stroke in India with 639,455 deaths and 6.4 million disability adjusted life years (DALY) lost.

In India the incidence of stroke is likely to rise in the coming years due to:

a. Increase in population
b. Increase in life expectancy
c. Rapid urbanization from migration of villagers to the cities
d. Changing lifestyles involving sedentary habits, smoking, excess alcohol use, etc.
e. Rising stress level in life

According to the estimates by the National Commission on Macroeconomics and Health, India, there will be 1.67 million stroke cases in India in 2015.

AGE AND STROKE INCIDENCE

Age has the strongest association with the incidence of stroke. For example, an 80 year old has about 30 times the risk of ischemic stroke than a

50 year old[3]. The age-specific incidence of stroke increases progressively with increasing age. In a systematic review of 15 population-based stroke incidence studies[4], the rate of total stroke for those aged less than 45 years ranged from 0.1-0.3 per 1000 person years, while for those aged 75-84 years, the range was 12-20 per 1000 person years in most studies. However, the impact of stroke on the individual family and society is strongest when it affects a young individual. Therefore, stroke in young attracts a large share of attention, perhaps disproportionately large. Therefore, in India as well as in other countries, there has been a large body of literature addressing the issues related to stroke in young. This review is an attempt to summarize some of this literature with special reference to the Indian context.

Clinical management as well as epidemiologic perspective raises several issues in relation to stroke in young. Important issues amongst these include the following:

a. Which age group should be included under the definition of ‘young’?
b. Are young Indians more susceptible to stroke than their counterparts in other countries, particularly western countries?
c. Are there age or sex-specific differences in the etiology of stroke between 'young' and 'older' adults? If so, are the differences quantitative, qualitative or both?
d. Which additional investigations are indicated for stroke in Indian young?
e. Are there specific genetic factors predisposing young Indians to stroke?

The age group included in studies on stroke varies widely in the reports published in literature. The lower limit of the age varies from 0 to 25 years in various reports with majority keeping it at 15 years. The upper age limit also varies from 40 to 55 years, majority being around 45 years. The wide variation compromises comparisons across the studies and confounds communication among experts. The rationale for the choice of age group is not given in the reports. The following points need consideration while defining the age category for young.

a. The unique set of causes affecting certain age groups has to be considered. This will allow identification of priority causes for the defined age group. In this context, rheumatic heart disease, peripartum stroke, arterial dissection and vascular malformations need special attention. All of these are exceedingly rare before the age of 15 years and after 50 years. A focus on the age group 15-50 years will allow estimation of the contribution of these causes to stroke in young.
b. Pregnancy-related causes of ischemic, hemorrhagic and venous strokes are unique to females in the reproductive age group. A large body of socioeconomic data in this age group has accumulated through a series of National Family Health Surveys (NFHS), the third one conducted in 2005-2006. This survey interviewed women aged 15-49 years and men aged 15-54 years. Thus, restricting the age group for 'stroke in young'

between 15 and 50 years would allow correlational studies with NFHS data.

c. Preventive strategies for the two common causes (rheumatic heart disease and pregnancy) of stroke in young and some others like infections related stroke need to be unique. Data and research in this age group would permit development of evidence-based strategies for prevention.

d. The latest estimates of 2006 indicate that the age group 15-49 years constitutes 52% of the population in India. Therefore, in our opinion, future studies may consider keeping 15-49 years (<50 years) as the age group for studies on stroke in young.

High Susceptibility of 'Young' Indians to Stroke

Several hospital-based studies on stroke in young adults from India had hypothesized that young Indians are more susceptible to stroke than their counterparts from industrialized countries. Older studies says: 'Indians as a whole are probably more susceptible to stroke than people in industrialized countries and that the magnitude of increased susceptibility is probably similar for the young and older adults … to answer this question, a well designed study is required in India which can be compared to a similar contemporary study in the west'. There are two recent studies[10] from Kolkata and Mumbai that allow us to compare the age-specific incidence between India and other countries. It is clear that young adults in India are not more susceptible to stroke than their

counterparts in the west, though Das *et al*[9] have noted that for all age groups together standardized rate of stroke incidence (123.5/100,000/year) is higher than that observed in USA (107/100,000/year), European countries (61-111/100,000/year), and Australia (99/100,000/year). These data, together with the studies on Indian immigrants to UK and the USA, suggest that Indians in general may probably be more susceptible to stroke but there is no age-specific higher susceptibility for the young. Previous hospital-based studies from India showing a high proportion of young strokes, ranging between 15 and 30%, were over estimates probably because of a preferential admission policy.

One area that remains to be well documented is the incidence of peripartum stroke. There is a strong impression among clinicians that the incidence is several times higher than that in other countries, particularly in industrialized countries.

Stroke Subtypes, Risk Factors and Etiology

The 'mix' of causes, the proportion with 'no cause' and the outcome of stroke in young varies from one series to the other. While some of the variations may be real, the majority is probably explained by the referral bias, differences in admission policy, in the pattern/availability of emergency services, investigation intensity and diagnostic criteria. All these may change with time as more causes are discovered and new diagnostic technologies become available. No two series are, therefore, strictly comparable. The following paragraphs may be read with this caveat in mind.

The prevalence of various risk factors in stroke in young has been analyzed in two studies from India[5]. In a case control study of young stroke patients (age group 15-45 years) with age and sex-matched hospital and community controls[6], prevalence of various risk factors was studied. Two hundred fourteen South Indian patients with first acute ischemic stroke and 99 hospital and 96 community controls were included. There was higher prevalence of smoking (odds ratio [OR] 7.77), systolic blood pressure (OR 1.88) and fasting blood glucose (OR 4.55) in patients. High density lipoprotein (HDL) was low and total cholesterol/HDL ratio was high in cases when compared with both hospital and community controls. A unit increase in the ratio of total cholesterol to HDL was associated with doubling of stroke risk. More than three components of metabolic syndrome were present in 12.6% cases when compared to 6% of community controls. Presence of ≥3 components of metabolic syndrome was also strongly associated with stroke(or 4.76). .

In another study in 1997, 177 patients with first ever ischemic stroke (age group 15-45 years) were included retrospectively based on hospital data, with 76% male and 24% female patients. Hypertension was present in 18% of the patients, whereas diabetes mellitus was present in 7% only. Sixty nine percent of male patients were smokers. Dyslipidemia in the form of elevated cholesterol was present in 17% and increase in triglycerides was observed in 42%patients.

Sridharan *et al*[23] analyzed the risk factors in ischemic stroke including the patients of all age groups. Hypertension, ECG abnormality, heart disease of any type, diabetes, smoking and alcohol were associated with stroke. Low HDL and low density lipoprotein (LDL) to HDL ratio was observed among stroke patients. South Asians living in UK are known to have an atherogenic lipid profile, which includes raised triglycerides, low HDL cholesterol and raised lipoprotein (a) level[24].

In a study of stroke in the young from Southeast Asia[16], the most common risk factors observed were hyperlipidemia (53.1%), smoking (49.8%), hypertension (45.8%) and a family history of stroke (29.3%). The presence of hyperlipidemia and hypertension was more commonly seen in patients with small vessel occlusion, large artery atherosclerosis and stroke due to unknown etiology, whereas hyperlipidemia was less commonly associated with caradioembolic stroke.

Analysis of prevalence of risk factors in studies of stroke in young from the west reveals prevalence of hypertension from 20 to 60%[18,19]. In Baltimore Washington Cooperative Young Stroke Study[12] examining 296 incident stroke cases in Black and White adults, hypertension was present in 61% of Black patients. Smoking was observed in 42.6% of White and 56.7% of Black men and 37.0% of White and 47.5% of Black women.

In Helsinki Young Stroke Registry[20] which included 1008 first ever patients of ischemic stroke in the age group of 15-49 years, hypertension, smoking and dyslipidemia with high total cholesterol emerged as important risk factors. The prevalence of hypertension increased with increasing age and was seen in 28.3% of patients in 15-44 year age group, whereas it was prevalent in 51.7% of patients in 45-49 year age group. Similarly, 38.4% of patients in 15-44 year age group and 54.5% in 45-49 year age group had increased level of cholesterol. Low HDL was present in 15.3 and 23.9% of the patients, respectively. Increased LDL was also present in 38.4% patients in 15-44 year age group and in 54.5% patients in 45-49 year age group. Smoking as a risk factor was observed in around 47% patients in both the age groups. It appears that the risk factor profile becomes similar to older population with increasing age, the change becoming more apparent at around 44 years of age.

In a study of 203 patients of stroke in age group of 15-45 years from Switzerland[19], hypercholesterolemia (39%) and smoking (46%) were important risk factors. However, hypertension was present in 19% patients only. Increased C reactive protein level was observed in 36% patients.

It appears that the risk factors for stroke in Indian population are not different from the western or Southeast Asian population. The traditional risk factors like hypertension, smoking and diabetes are associated with stroke in both young and elderly. The role of dyslipoproteinemia in the pathogenesis of cerebrovascular disease is less certain than that of coronary artery disease;

however, increased total cholesterol and increased triglyceride levels have been observed in patients from India and Southeast Asia. Increased level of total cholesterol has been associated with ischemic stroke in young in most of the populations and it does not significantly differ from the Indian subcontinent.

In a study on stroke in young from Sri Chitra Tirunal Institute of Medical Sciences and Technology (SCIMST), Trivandrum[6], patients of ischemic stroke were classified based on Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria; 25.2% patients had cardioembolic stroke, 12.6% had large artery atherosclerosis and 7.5% had lacunar infarcts. Strokes due to other determined etiology were 11.2% (7.0% arterial dissection, and one patient each with lupus erythematosus, primary antiphospholipid antibody syndrome and protein S deficiency). Four patients had stroke due to other causes (one case each of Moya moya disease, Takayasu's arteritis, fibromuscular dysplasia and nephritic syndrome).

Data from several studies indicate that 21-48% of strokes in the young are caused by atherosclerotic large artery occlusive disease, 10-33% are due to nonatherosclerotic large artery occlusive disease (dissections have comprised 10-20% in some studies), 13-35% are caused by cardioembolism, 3-18% by penetrating artery disease, 8-15% by prothrombotic states and 4-15% by miscellaneous causes. Cryptogenic stroke comprises 7-40% of the cases. In a study by Lee *et al*[16] vascular risk factors like hypertension, diabetes,

hyperlipidemia were seen more commonly in patients with large artery atherosclerotic disease or small vessel occlusive disease.

Cervical artery dissection was one of the relatively common causes of stroke in young. Various studies report that around 6-15% of the patients had carotid artery dissection. Carotid and vertebral artery dissection were seen with a variable frequency. In one study, 24 patients had arterial dissection of 170[16] patients who underwent angiographic studies, with carotid dissection in 13 and vertebral dissection in 11. The commonest site for carotid dissection was just above the carotid bifurcation. Putaala *et al*[20] in a study of stroke in young from Helsinki, reported that 59% of patients with stroke of other determined etiology had cervical or intracranial artery dissection. Out of 155 patients with dissection, 80 had vertebral artery dissection and 67 had internal carotid artery dissection. Other causes of stroke like antiphospholipid antibody syndrome, factor V Leiden mutation, proteins C and S deficiency, antinuclear antibody positivity, systemic lupus erythematosus, fibromuscular dysplasia, migraine-related stroke and other vasculitis were observed in 1-2% of patients.

The common causes of cardioembolic stroke include rheumatic heart disease, paradoxical embolism due to patent foramen ovale (15-37% of cardioembolic strokes), atrial fibrillation (10-14% of cardioembolic strokes), mitral valve prolapse (1-38%), mechanical prosthetic valves, dilated cardiomyopathy, atrial myxoma, congestive heart failure and sick sinus syndrome.

Genetics

Several candidate genes have been found to be associated with stroke. Angiotensin converting enzyme (*ACE*) insertion/deletion polymorphisms, methylenetetrahydrofolate reductase (*MTHFR*) mutations, apolipoprotein E polymorphisms and phosphodiesterase 4D (*PDE4D*) gene variants have been studied in Indian population.

In a case control study, apolipoprotein E genotypes were studied in patients of stroke[34]. A high frequency of apo ε 4 allele (30% in cases and 11% in controls) was observed (OR 4.2). The authors concluded that presence of apo ε 4 allele along with elevated triglycerides, hypertension and age could predict the development of stroke. In another case control study from Hyderabad,[35] angiotensin converting enzyme deletions/insertions were studied. The ORs for ID genotype, DD genotype and D allele as an independent risk factor for ischemic stroke were 2.89, 3.68 and 2.13, respectively. Presence of D allele was also associated with intracranial atherosclerosis.

MTHFR C677T mutations were studied in patients with both arterial and venous stroke with elevated homocysteine levels.[36] The prevalence of the mutated homozygous and heterozygous *C677T MTHFR* genotype in the patients with arterial stroke was 1.4 and 31.88%, respectively. Their frequency was 16.6 and 33.3% in venous stroke. The genotyping results from controls showed that there was only one heterozygote out of the 49 studied. The

mutated allele was present in 25.4% of patients in age group of 15-50 years. OR for the probability of the *C677T MTHFR* gene mutation in the patients versus control group was 22.29 indicating that *C677T MTHFR* mutation is strongly associated with arterial stroke especially in young adults.

PDE4D gene seems to contribute to the risk of stroke in carriers independent of other genetically based risk factors.[37] The association of *PDE4D* with stroke was investigated in a South Indian population.[38] *PDE4D* gene polymorphisms were studied in 250 cases and controls. Single nucleotide polymorphism (SNP) 83 showed significant association with stroke in the population under study, whereas SNPs 87 and 32 were monomorphic. SNP 83 was found to be significantly associated with two stroke subtypes, intracranial large artery atherosclerosis (the most frequent subtype in the population) and small artery occlusion. The role of *G20210A* in ischemic stroke patients was studied in a case control study from South India.[39] None of the study subjects were either heterozygous or homozygous for this gene mutation as indicated by polymerase chain reaction (PCR) analysis. *ACE* gene polymorphism is presently being studied in patients of both ischemic and hemorrhagic stroke with age-matched controls. The above studies point toward an association between *ACE* gene mutations, *MHTFR* mutations and *PDE4D* polymorphisms with Homocysteine.

Cerebrovascular diseases characteristic of each age period

1. Prenatal circulatory diseases leading to:
    a. Porencephaly
    b. Hydranencephaly
    c. Hypoxic-ischemic damage
    d. Unilateral cerebral infarction
2. Perinatal and postnatal circulatory disorders resulting in:
    a. Cardiorespiratory failure and generalized ischemia—*e´tat marbre*
    b. Periventricular infarcts
    c. Matrix hemorrhages and ischemic foci in premature infants
    d. Hemorrhagic disease of the newborn
3. Infancy and childhood: vascular diseases associated with:
    a. Ischemic infarction
    b. Congenital heart disease and paradoxical embolism
    c. Moyamoya
    d. Bacterial endocarditis, rheumatic fever, lupus erythematosus
    e. Sickle cell anemia
    f. Mitochondrial disorders (MELAS)
    g. Homocystinuria and Fabry's angiokeratosis

4. Adolescence and early adult life: vascular occlusion or hemorrhage with:

    a. Pregnancy and puerperium

    b. Estrogen-related stroke

    c. Migraine

    d. Vascular malformations

    e. Premature atherosclerosis

    f. Arteritis

    g. Valvular heart disease

    h. Sickle cell anemia

    i. Antiphospholipid arteriopathy, plasma C-protein deficiency and other coagulopathies.

    j. Moyamoya, Takayasu disease

    k. Arterial dissections

    l. Amyloid angiopathy

5. Middle age:

    a. Atherosclerotic thrombosis and embolism

    b. Cardiogenic embolism

    c. Primary (hypertensive) cerebral hemorrhage

    d. Ruptured saccular aneurysm

    e. Dissecting aneurysm

    f. Fibromuscular dysplasia

6. Late adult life:

    a. Atherosclerotic thrombotic occlusive disease

    b. Embolic occlusive disease

    c. Lacunar state

    d. Brain hemorrhage (multiple causes)

    e. Multi-infarct dementia

    f. Binswanger disease

PREVALENCE OF VARIOUS AETIOLOGIES IN PATIENTS WITH STROKE IN YOUNG

	Age Group	Patient No.	LAA	SVO	CE	ODE/Venous thrombosis	UDE
Bansal et al., (India) 1973	**15 – 45**	**177**	**24**	**NM**	**17**	**0.6**	**36**
Chopra et al., (India) 1979	**<40**	**182**	**60**	**NM**	**15**	**22.5**	**NM**
Dalal et al., (India) 1979	**<45**	**81**	**51**	**NM**	**42**	**7**	**NM**
Radhakrishnan et al., (Libya) 1986	**15 – 40**	**63**	**54**	**NM**	**21**	**3**	**22**
Bougousslavsky et al., (Switzerland) 1987	**16 – 29**	**41**	**5**	**NM**	**29**	**5**	**10**
Chanellor et al., (New Zealand) 1989	**<40**	**66**	**NM**	**NM**	**7.5**	**3**	**32**
Lanzino et al., (Italy) 1991	**16 – 45**	**155**	**31**	**NM**	**3**	**3**	**40**
Lisovosky et al., (France) 1991	**5 – 40**	**148**	**22**	**NM**	**13**	**NM**	**20**
Leno et al., (Spain) 1993	**<50**	**81**	**30**	**NM**	**17**	**NM**	**NM**
Adams et al., (Lowa, USA) 1995	**15 – 44**	**329**	**21.6**	**8.2**	**19.5**	**24.5**	**25.7**
Nayak et al., (India) 1997	**15 – 45**	**177**	**24**	**NM**	**17**	**22**	**36**
You et al., (Australia) 1997	**15 – 55**	**201**	**52**	**22**	**10**	**NM**	**15**
Kristensen et al., (Sweden) 1997	**18 – 44**	**107**	**12**	**4.6**	**33.1**	**30.7**	**19.6**
Kittner et al., (Baltimore, USA) 1998	**15 – 44**	**428**	**2**	**10**	**15**	**35**	**38**
Leys et al., (France) 2002	**15 – 45**	**287**	**8.4**	**1.7**	**5.2**	**22.3**	**62.4**
Jacobs et al., (Manhattan, USA) 2002	**20 – 44**	**74**	**15**	**18**	**6**	**6**	**55**
Lee et al., (Taiwan) 2002	**15 – 45**	**241**	**7.9**	**22.4**	**19.5**	**24.5**	**25.7**
Lipska et al., (India) 2007	**15 – 45**	**214**	**12.6**	**7.5**	**25.2**	**11.2**	**43.5**
Putaala et al., (Finland) 2009	**15 – 49**	**1008**	**7.5**	**13.8**	**19.6**	**26.0**	**31.0**

LAA – Large artery atherosclerosis; SVO – Small vessel occlusive disease; CE – Cardioembolism;
ODE – Other determined etiology, UDE – Undetermined etiology, NM – Not mentioned

First line investigations for stroke in young
- Computed tomography/Magnetic resonance imaging of brain
- Complete blood count with differential and platelet count
- Prothrombin time, INR, activated partial thromboplastin time
- Blood glucose, serum electrolytes, blood chemistries
- Lipid profile
- Erythrocyte sedimentation rate
- Pregnancy test (in females)
- Chest roentgenogram
- Electrocardiogram
- Transthoracic echocardiography
- Duplex scanning of the cervicocephalic vessels

Second line investigations
- Transesophageal echocardiography
- Magnetic resonance angiography and venography
- Cerebral angiography
- Anticardiolipin antibody
- Antinuclear and other autoantibodies (ANCA, Anti-SSA, Anti-SSB, Rheumatoid factor)
- Protein C and S, antithrombin III, activated protein C resistance
- Hemoglobin electrophoresis and sickle cell testing
- Serum homocysteine
- HIV serology
- Serologic tests for syphilis
- Blood/cerebrospinal fluid lactate
- Factor V Leiden mutation

Other investigations (depending on clinical findings or above test results)
- Holter monitoring
- Investigations for coronary artery disease
- Fibrin degradation products
- D-dimer assay
- Serum angiotensin converting enzyme assay
- Plasma lactate and pyruvate level

TABLE 5. Potential New Risk Factors for Ischemic Stroke

- Genetic factors/genotypes
  - Angiotensin-converting enzyme genotype
  - Factor V Leiden
  - Prothrombin G20210A
  - MTHFR
  - Human platelet antigen type 1
  - Factor XIII
  - Apo E
  - Plasminogen activator inhibitor-1 4G/5G genotypes
  - Phosphodiesterase 4D
  - 5-Lipooxygenase–activating protein
- Inflammatory markers
  - Leucocyte count
  - Monocyte count
  - High-sensitivity C-reactive protein
  - Soluble CD40 ligand
  - Serum amyloid A
  - Interleukins (IL-6, IL-18)
  - Vascular and cellular adhesion molecules
  - Myeloperoxidase
  - Matrix metalloproteinase-9
- Infectious agents
  - Cytomegalovirus
  - Herpes simplex virus
  - *Chlamydia pneumonia*
  - *Helicobacter pylori*
  - *Legionella* sp
  - Periodontal disease
- Lipid-related factors
  - Small, dense LDL
  - Lipoprotein (a)
  - Remnant lipoproteins
  - HDL subtypes

Lipoprotein-associated phospholipase A2

Adiponectin

Oxidative stress

Oxidized LDL

Biomarkers of hemostasis/thrombosis/impaired fibrinolysis

Fibrinogen

Protein Z

Von Willebrand factor antigen

Plasminogen activator inhibitor-1

Tissue-type plasminogen activator

Factors V, VII, and VIII

D-dimer

Fibrinopeptide A

Prothrombin fragment 1 and 2

Antiphospholipid antibodies

Platelet-related factors

Platelet aggregation

Platelet activity

Platelet size and volume

Functional markers

Endothelial dysfunction

Arterial compliance, elasticity, stiffness (e.g., pulse pressure)

Ankle-brachial systolic pressure index

B-type natriuretic peptide

Microalbuminuria

Ctstatin C

Studies are being done on the following markers

Biomarkers	General Features	Ischemic Stroke Studies
BNP	Vasoactive peptide hormone Natriuretic, diuretic, and vasodilator activity Cardiac and cerebral origin	↑ BNP in acute phase ↑ BNP predicts poststroke mortality
DD	Products of degradation of fibrin Marker of hemostatic imbalance	↑ DD in acute, subacute, and chronic phases ↑ DD in cardioembolic stroke Predictor of new vascular events and prognostic role
S100b	Calcium-binding protein Synthesized in astroglial cells Marker of brain damage	↑ S100b in acute phase S100b associated with clinical deficit, infarct volume, and functional disability
RAGE	Transmembrane receptor Immunoglobulin superfamily Expressed by endothelial cells, mononuclear cells, and neurons Overexpressed at sites of vascular damage sRAGE have antiatherogenic effects	↑ RAGE in acute, sub acute and chronic phases
CRP	Pentraxin Acute-phase protein; participates in the systemic response to inflammation Hepatic and extrahepatic synthesis	↑ CRP in acute phase Predictor of risk of cerebrovascular events Prognostic value after stroke
MMP-9	Proteolytic enzyme Involved in tissue remodeling Important role in neuroinflammation	↑ MMP-9 in acute phase ↑ MMP-9 associated with hemorrhagic transformation Correlated with infarct size and clinical deficit

Chimerin	Nonprotein kinase C (GAP family) Synthesized by neurons (α1 isoform) Regulatory function in actin repolymerization (neurocytoskeleton)	↑ chimerin in acute phases
Secretagogin	Calcium-binding protein Expressed in neuroendocrine cells Marker of neuronal death	↑ Secretagogin in acute phase
Neurotrophin -3	"Neuronal survival factor" (neurotrophin family of growth factors)	Endogenous neurotrophin-3 enhances neuronal injury during acute stroke ↓ Neurotrophin-3 synthesis has neuroprotective role
Caspase-3	Cysteine protease "Executioner" in apoptosis	Activation of caspase-3 in permanent and transient brain ischemia Caspase activation after ischemia-induced brain damage

- BNP : Brain Natriuretic Peptide
- DD : D-Dimer
- RAGE : Receptor for advanced Glycosalated end Products
- CRP : C-Reactive Protein
- MMP : Matrix Metallo Proteinase

Still experiment has to be done to reveal lot other significant biomarkers for stroke.

HOMOCYSTEINE

Cardiovascular morbidity and mortality is expected to rise exponentially in developing countries due to the epidemiological transition[43] that these countries are going through currently. It is this magnitude of the problem which has forced the Indian scientists to look for preventive aspects to curb the increasing mortality through cardiovascular diseases. In this context, Homocysteine plays a role in being easily reversible risk factors for atherosclerosis.

Homocysteine Metabolism:

Homocysteine metabolism is greatly impacted by enzyme function, lifestyle choices and nutritional status.

Gender and Genetics:

Women tend to have lower basal levels than men and neither contraceptives nor Hormone replacement therapy seem to alter their levels significantly.

Epidemiological evidence has shown homocysteine levels to be over 45% lower in westernized adult black Africans than in age-matched white adults, revealing racial genetic differences in homocysteine metabolism.

Lifestyle

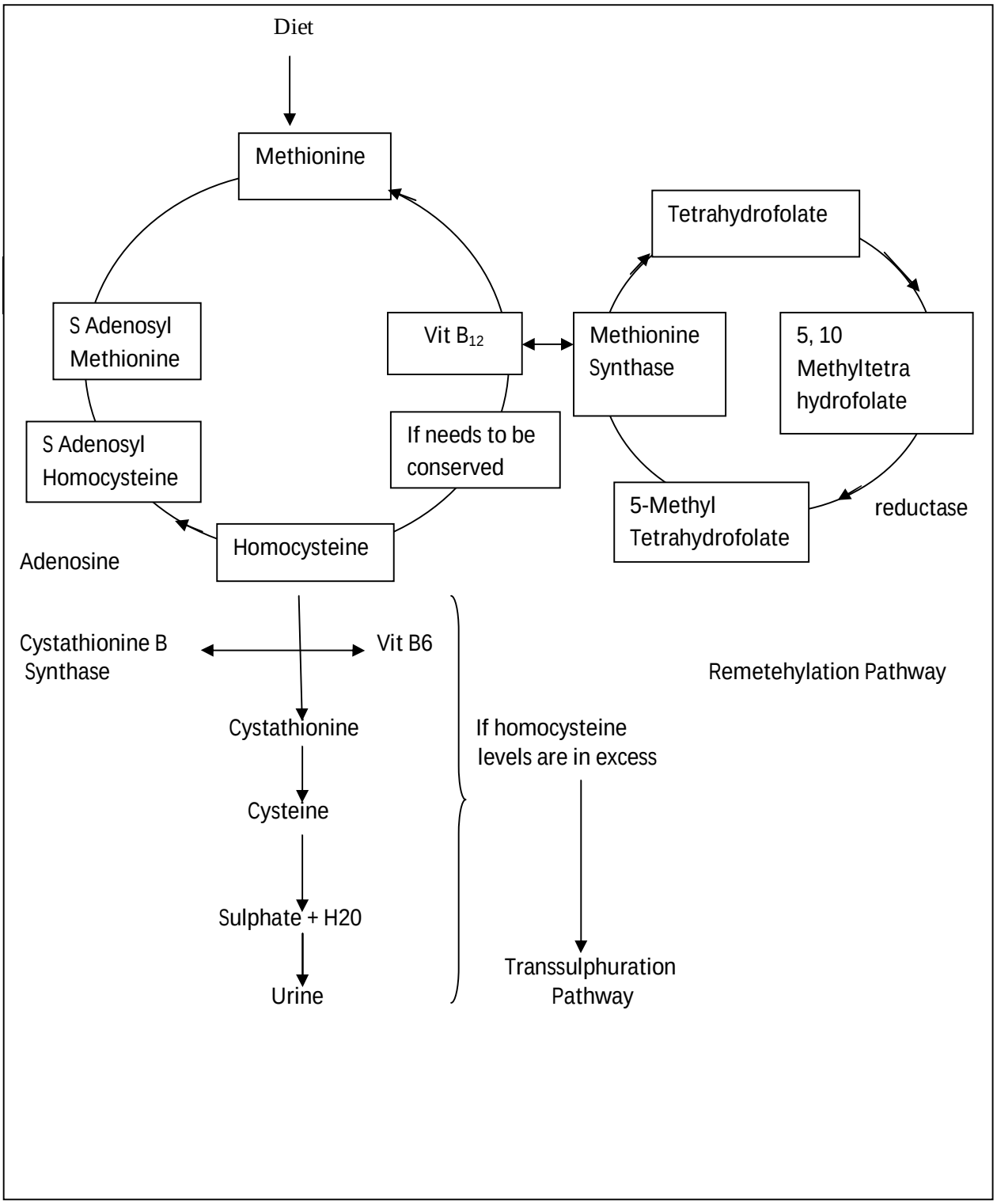
A marked positive dose-response relation between coffee consumption and plasma Homocysteine levels was observed. Cigarette smoking and chronic ingestion of alcohol has also been associated with increased homocysteine levels.

Nutritional considerations and metabolism

Those individuals in the lowest quartiles for serum folate and vitamin B12 have significantly higher concentrations of homocysteine. Those having lowest quartile of serum pyridoxal 5^{43} phosphate(p5p – the bioactive form of vitamin B6) also have increased homocysteine concentrations. The various metabolic steps where these vitamins play a role is depicted in Fig.

1. The first step in the synthesis of homocysteine is the formation of S-adenosyl methionine (Adenometh), an important methyl donor, from methionine. Adeno-metho is then converted to SA denosyl homocysteine (Adeno-Hcy), which is further hydrolyzed to yield homocysteine and adenosine depending on whether there is a relative excess or a deficiency of methionine, homocysteine may then enter either transulphuration or remethylation pathways.

HOMOCYSTEINE METABOLISM



1. Remethylation

In the remethylation cycle, homocysteine is salvaged by the acquisition of a methyl group in a reaction catalyzed by methionine synthase, NS-methyl-tetrahydrofolate is the methyl donor in this reaction, and N5, N10 – Methylene tetrahydrofolate reductase functions as a catalyst in the remethylation process.

2. Transulphuration

Under conditions in which an excess of methionine is present or cysteine synthesis is required,homocysteine enters the transulphuration pathway. In this way, homocysteine condenses with serine to form cystathionine in a reaction catalyzed by the vitamin B6 – dependent enzyme cystathionine B synthase. Cystathionine is subsequently hydrolysed to form cysteine, which may then be incorporated into glutathione and further metabolized to sulphate and excreted in the urine.

HYPERHOMOCYSTEINE REFERENCE RANGE

Sex	Age	Lower limit (micromol/litre)	Upper limit (micromol/litre)
Female	12–65 years	3.0	12.0
	>65 years	15.0	20.0
Male	12–65 years	6.0	15.0
	>65 years	15.0	20.0

Kang and co-workers have classified Hyperhomocysteinaemia as follows:

Mild : 15 – 30 micromole per litre
Moderate: 30 – 100 micromole per litre
Severe : > 100 micromole per litre

In some subjects, fasting levels may be in the normal range, but high plasma Homocysteine level may be seen after a methionine loading test. Plasma homocysteine levels may be altered by both inherited and acquired factors (Table – 1).

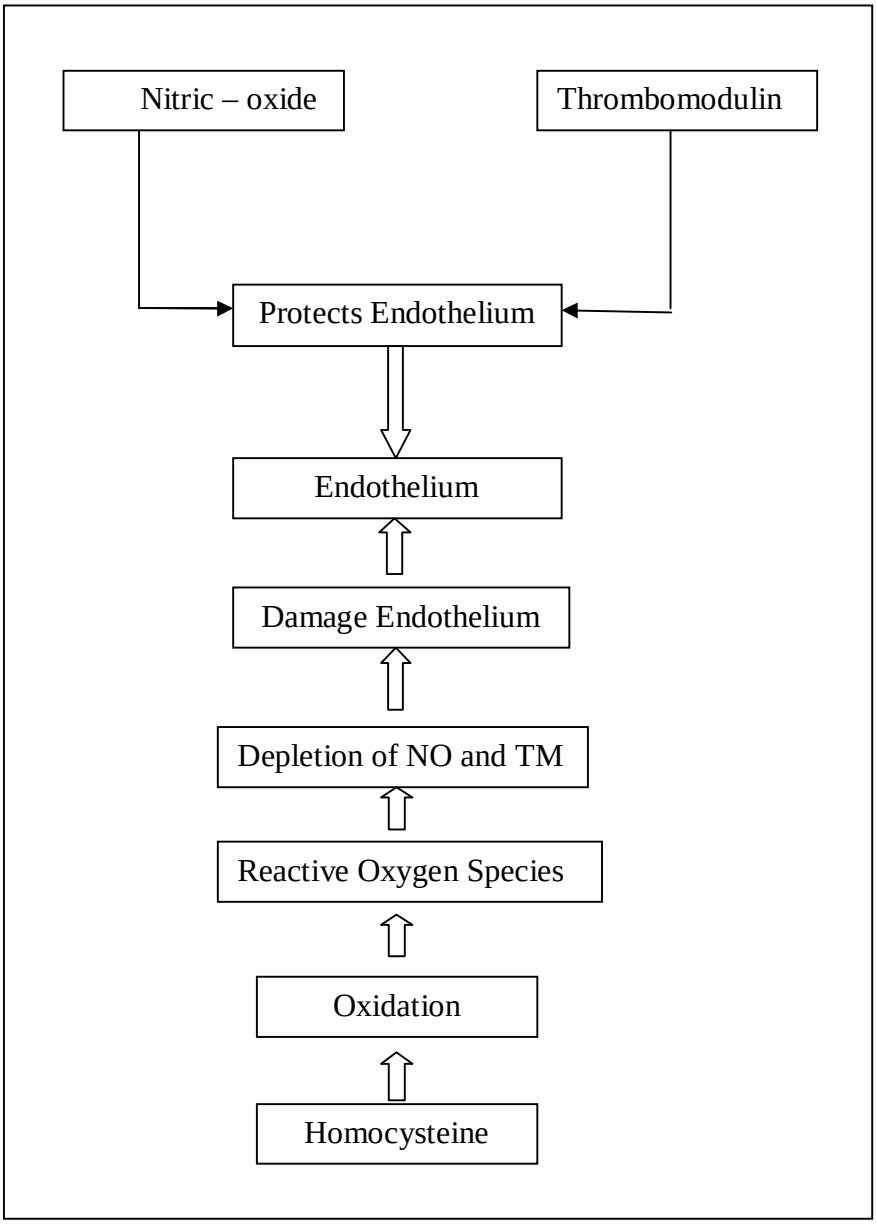
Table – 1

Factors influencing homocysteine metabolism

Inherited Enzyme	Deficiencies in the metabolic pathway (cystathionine B synthase, 5, 10 – Methylene tetrahydrofolate reductase, methionine synthase)
Age and sex	Advancing age, male sex, menopause
Nutritional deficiencies	Folic acid, vitamin B6 and B12
Disease Status	Renal failure, malignancies, psoriasis, rheumatoid arthritis, Systemic lupus eythematosus, hypothyroidism, diabetes mellitus.
Medications	Metformin, methotrexate, anticonvulsants, niacin and theophylline, decreased levels of betaine

Total homocysteine encompasses protein bound and unbound fractions, with 80% being in the bound state. The term homocysteine referes to combined pool of homocysteine, a mixed disulphide. Homosysteine and risk of cardiovascular disease cross – sectional studies have consistently demonstrated an association between blood levels of homocysteine and the anatomic extent of atherosclerotic vascular disease in the coronary, cerebral and peripheral circulation. In 1995, Boushey[52] et.al. performed a meta analysis of 27 observational studies involving about 4000 patients. An elevated blood level of homocysteine was associated with an increased risk of vascular events in the coronary (odds Ratio – OR : 1.7),cerebral (Or : 2.5) and peripheral (OR :6.8) circulations. It was estimated that around 10% of coronary heart disease deaths in middle aged men might be prevented by a 5 micromol/L reduction in blood levels of homocysteine. Thus proving the fact that the magnitude of risk was similar to that for elevated cholesterol.Knekt[53] et.al. studied total homocysteine level for its prediction of major coronary artery disease events among women. A total of 74 and 75 major coronary events which occurred in women with and without known heart disease, respectively, during a 13 year follow-up were studied. Amongst women with baseline heart disease, the relative risk of such events, adjusted for age, smoking, hypertension, diabetes, serum cholesterol and body mass index was 3.32 in the highest homocysteine quartile compated with the lowest quartile. Amongst women free of heart disease of baseline, the corresponding relative risk was 0.77.

Mechanism of Homocysteine Induced Vascular Damage



Pathogenesis of vascular disease[54]

There are numerous studies which have explored sites of adverse influence of homocysteine,including the endothelial surface, vascular smooth muscle cells,connective tissue, interactions with plasma lipoproteins, clotting factors and platelets. The endothelium has received considerable attention as the final common pathway of homocysteine induced vascular injury.

Endothelium in health regulates vascular tone by modulating endothelium – derived relaxing factor (nitric oxide : NO). It also modulates the coagulation cascade through protein C and antithrombin III interactions. By influencing tissue plasminogen activator it also has fibrinolytic functions. It also controls the composition of the subendothelial matrix and smooth muscle cell proliferation. Many of these normal properties may become deranged in the presence of elevated homocysteine levels.

Plasma homocysteine and coronary artery disease risk in Indians

Though the casual role of homocystiene in the genesis of atherosclerosis is getting established in the recent past yet there are conflicting statements made about its role and implications in the disease process. The researchers in their study have demonstrated that though the levels of homocysteine have been found to be elevated in various atherosclerosic events yet there is no solid evidence to correlate the two. The finnish population study[56], the multiple risk factor intervention trial (MRFIT)[57] and the atherosclerosis in communities (ARIC)[58] study did not show any relation of plasma homocysteine levels to cardiovascular disease. One provocative view holds that hyperhomocysteinaemia, instead of being an antecedent of cardiovascular events, may be a markers of tissue damage or repair following them[59].

Contrast to above statement there are several other recent studies who have investigated and confirmed the contribution of homocysteine to cardiovascular disease (CVD) risk both among immigrant Indians[60] and those living in India[61]. Chambers et al conducted two parallel case control studies, one in Europeans and the other in Indians, to evaluate fasting and postmethionine load homocysteine as risk factor for cardiovascular disease. They found that elevated plasma homocysteine levels were independently associated with cardiovascular disease in both UK Indians and Europeans. They showed that the odd ratio for coronary heart disease for a 5 mmol/L increment in plasma homocysteine was 1.3 in Europeans and Indians. However, the Indians in this study were not evaluated for the other known associations of cardiovascular disease characteristic of Indian ethnicity, namely abnormal waist-hip ratio (WHR), raised Lipoprotein (a) and hyperinsulinemia. The strength of this association, after correction for these potentially confounding risk variables, would have provided better insight into the place of homocysteine in the risk factor spectrum. In a population study from Canada involving nearly a thousand participants from three ethnic groups (South Asians, Europeans and Chinese), the presence of clinical cardiovascular disease and carotid intimal medial thickness measured by B-mode ultrasound were correlated with conventional and non-conventional risk factors[62]. Even the South Asians had significantly higher levels of plasma homocysteine than their European and Chinese counterparts, this did not translate into an independent association of homocysteine with cardiovascular disease.

In a population based Study of South Asians in Canada[63] and a case-control Study of Asians living in the UK[64] have shown that Indians tend to have higher homocysteine levels as compared to European and Chinese population. This could be attributed to the reduced intake of vitamin B12 in Indians and the prolonged cooking of vegetables which has been observed in some Indian households in the UK.

Though there is lot of emphasis given to the casual relationship of hyperhomocystenimia to cardiovascular disease the other components of vascular involvement should not be ignored as they also contribute for significant morbidity and mortality.

Homocysteine: A new emerging risk factor for hypertension

Vascular endothelium does play a critical role in the control of blood pressure. There is a very optimal balance between the vasocontrictive and vasodilator factors acting on the vessel wall and thus contributing for its tone. Mendis et al[65] in their study conducted in Sri Lanka demonstrated the association between hypertension and homocysteine levels. Serum homocysteine were measured in 86 patients with a diagnosis of essential hypertension and compared with those of an age and sex matched group. They found that patients with hypertension had significantly higher mean serum concentrations of homocysteine. Bortolotto LA et al[66] demonstrated that hypertensive patients with high levels of homocysteine are associated with

increased arterial stiffness (measured by aortic distensibility and homocysteine levels can help in cardiovascular risk assessment in hypertensive population.

Adunsky et al[67] studied the distribution of total homocysteine levels in a sample of older patients consecutively admitted following acute ischemic cerebral stroke, as compared with healthy controls. 137 stoke patients and 132 healthy controls (Age 0.06 = 60 years) participated in this study. The results showed that stroke patients (mean age 74 years) had higher homocysteine levels as compared with controls (13.8 and 9.8) respectively.

Peripheral vascular disease

Elevated homocysteine levels have been established as an independent risk factor for intermittent claudication and deep vein thrombosis. A four-fold increase in risk of peripheral vascular disease was noted in individuals with hyperhomocysteine levels[68]. An increased risk of peripheral vascular occlusion has been noted in women taking oral contraceptives, which might be lined to the significantly increased homocysteine levels in women so affected[69].

In one survey conducted by NIMHANS, doctors found that 40 per cent of stroke patients under 40 had high levels of homocysteine compared to only 17 per cent normal people found to have high levels of this amino acid.

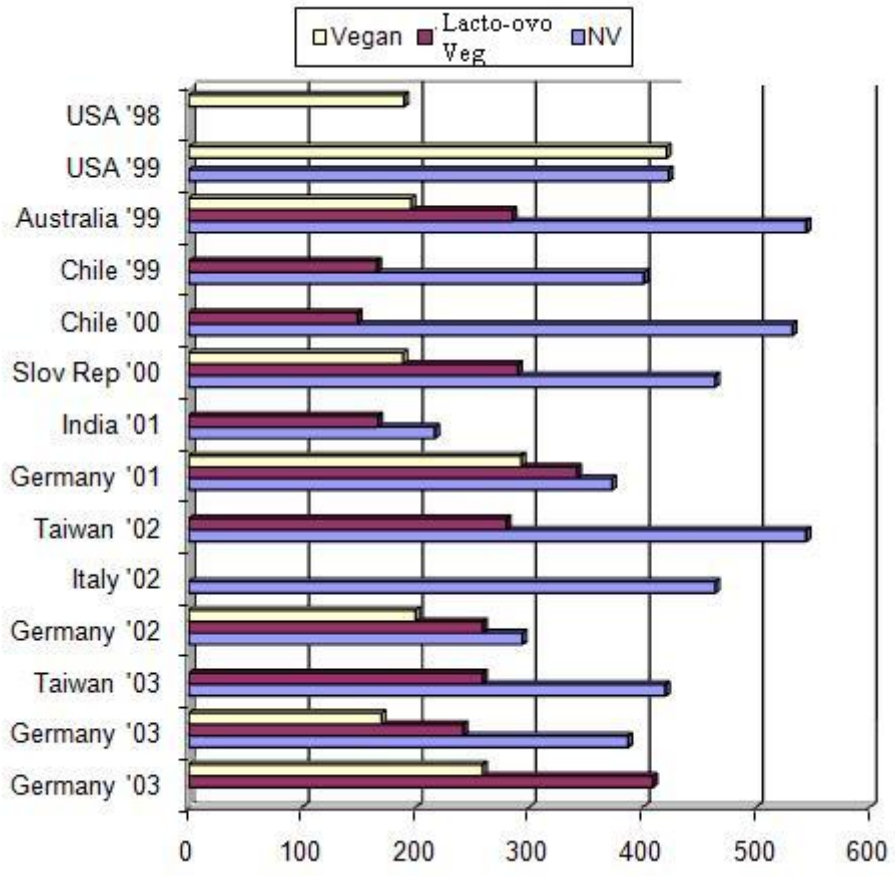
Homocysteine levels in Vegetarians and Non-vegetarians:

Studies[72,73] have shown elevated homocysteine in people who are on strict vegetarian diet since childhood. Reason attributed are decrease amount of Vit.B12 in their diet. But the difference between homocysteine in vegetarians and non-vegetarians are not gross. Because, vegetarians may get Vit.B12 from milk or from bacterial contaminants in vegetables and fresh fruits as they carry significant amount of Vit.B12. Other food substances[71] which have some Vit.B12 are soya beans, legumes, cottage cheek.

Various studies have shown values of homocysteine in non-vegetarians is between 10 – 13 micromol/L[70,72,73] and in vegetarians is between 12 – 15 micromol/L[70,72,73]. Some studies have shown increased incidence of acute vascular events (especially stroke) in vegetarians when compared to non-vegetarians[71]. Still lot of evidence is required to prove this issue.

At least 14 studies have measured the homocysteine levels in vegetarians. The following diagram shows the blood B12 levels of the participants of 13 of those studies (one did not report B12 levels[70]).

Serum B12 Levels in Homocysteine Studies on Vegetarians (pg/ml)



A - Most of these vegetarians did not supplement their diets with B12. USA '98[5], USA '99 (averaged 5.6 µg B12/day)[6], Australia '99[7], Chile '99[8], Chile '00[9], Slovak Republic '00[10], India '01[11], Germany '01[12], Taiwan '02[13], Italy '02[14], Germany '02[15], Taiwan '03[17], Germany '03[18], Germany '03 (took "B vitamins", amounts not reported)[18]

Normal B12 levels are from 200 to 900 pg/ml. The above diagram shows that vegans had the lowest B12 levels, followed by lacto-ovo-vegetarians, and then non-vegetarians.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study Population:

Total of 50 patients with stroke in young were enrolled for the study. Patients were selected from medicine wards of the Institute of Internal Medicine.

Patients are selected for the study who satisfied all the inclusion and exclusion criteria. Written consent was obtained from all the patients/care providers.

Study Duration:

This study was conducted for a period of eighteen months from January 2009 to June 2010.

Study Design:

Cross – Sectional Study.

Methods:

Detailed clinical history was taken from each patients and a complete review of their case notes performed. A complete clinical examination of the nervous system and cardiovascular system was done for each patient.

Laboratory Study

To all selected cases, following investigations were taken:

1. Complete Blood Count.

2. Renal Function Test

3. Liver Function Test

4. Prothrombin Time / INR

5. Activated Partial Thromboplastin Time

6. ECG

7. Echocardiography

8. CT Brain

9. Fasting Blood Sugar

10. Fasting Lipid Profile

11. Thyroid Function Test

12. Carotid & Vertebral Doppler (4 Vessel Doppler)

13. ELISA (HIV)

14. VDRL (Syphilis)

15. Rheumatoid Factor

16. Anti-nuclear Antibodies

17. Pregnancy Test

18. Fasting Plasma Homocysteine
(Using photometric analysis)

19. Other relevant investigations.

Inclusion Criteria

1. Age > 12, $\leq$ 40

2. Ischemic Stroke

Exclusion Criteria

1. Age $\leq$12, > 40

2. Hemorraghic Stroke

3. Smoking

4. Alcoholism

5. Known Systemic Hypertension

6. Diabetes Mellitus

7. Cardiac Disease

8. Peripheral Vascular Disease

9. Renal Disease

10. Hypothyroidism

11. Drugs which interfere with Homocystine Metabolism (Anti-Epileptics, Anti-Chemotherapeutic Drugs, Methformin Theophylline Niacin and others)

12. Dyslipidemia

13 . Other Inflammatory States, Systemic Lupus Erythematosus Rheumatoid Arthritis, Psoriasis

14. Patient with previous history of stroke

Statistical Analysis

The significance value is found using standard error of mean and student T test. The final results were obtained using SPSS software. Variables were considered to be significant if ($P < 0.05$)

OBSERVATION AND RESULTS

OBSERVATIONS

S.No.	Baseline Features	Total Number
01.	Male	42
02.	Female	08
03.	Non-vegetarians	41
04.	Vegetarians	05
05.	Family History	05
06.	Death	03 (2 Males, 1 Female)

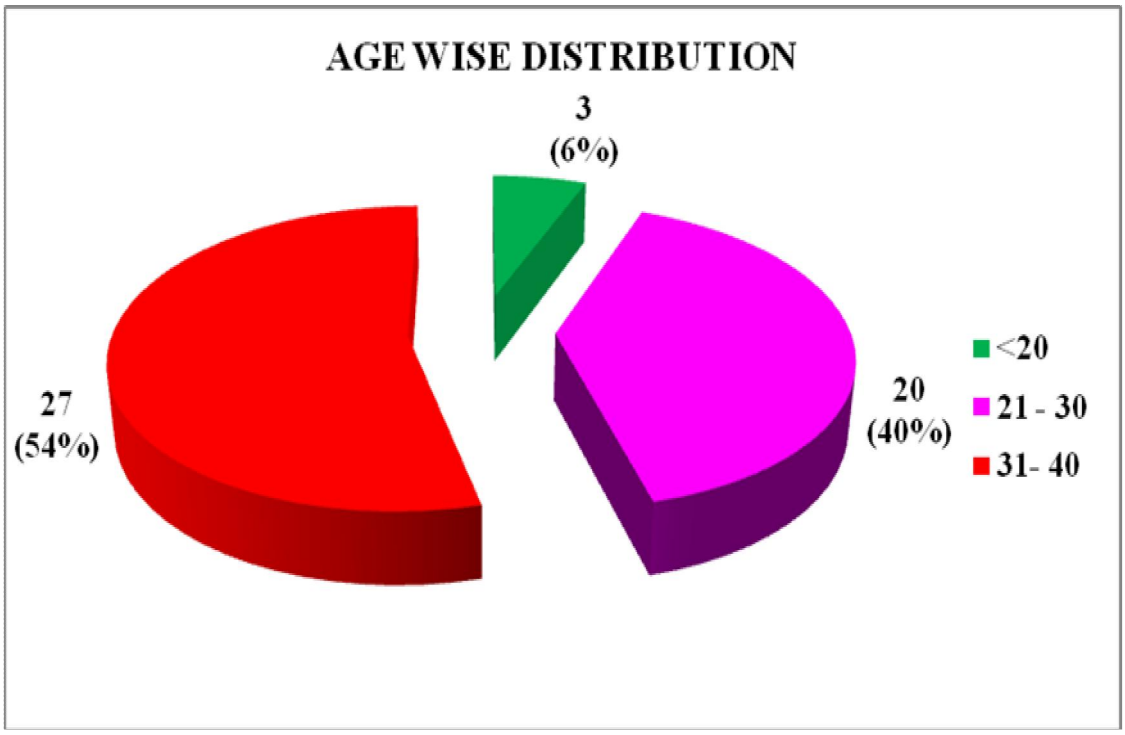
AGE WISE DISTRIBUTION OF STROKE

Age group	No. of patients	Percentage
<20	03	06%
21 - 30	20	40%
31- 40	27	54%

3 patients (6%) are below age 20

20 patients (40%) are between age 21 to 30

27 patients (54%) are between age 31 – 40

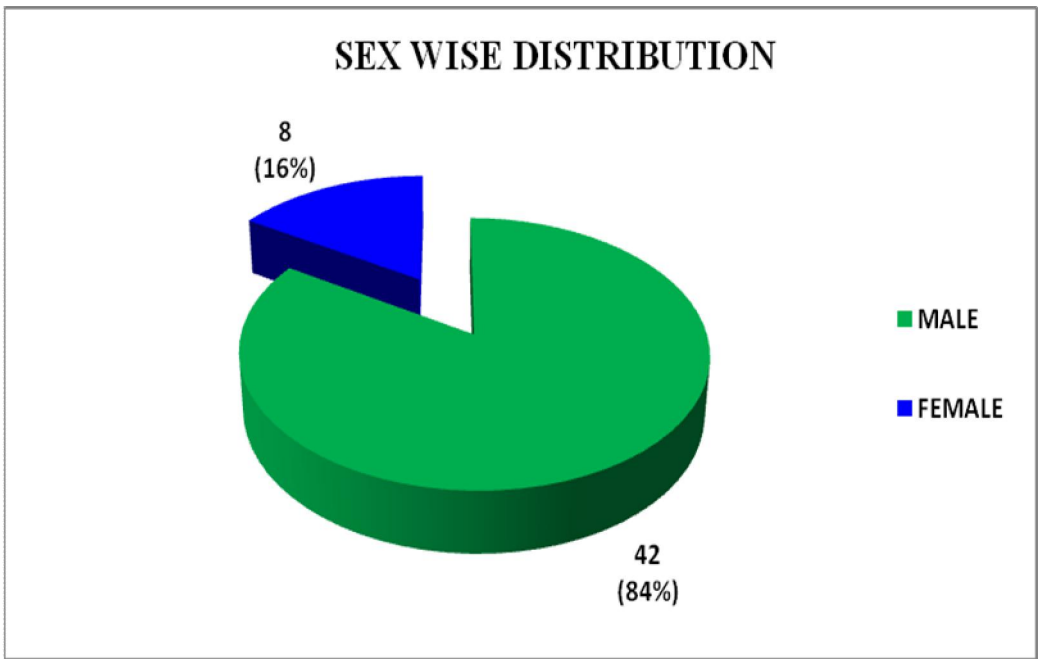


SEX WISE DISTRIBUTION OF STROKE

	MALE	FEMALE
NO. OF PATIENTS	**42**	**8**
Percentage	**84%**	**16%**

42 Patients (84%) are males

8 patients (16%) are females

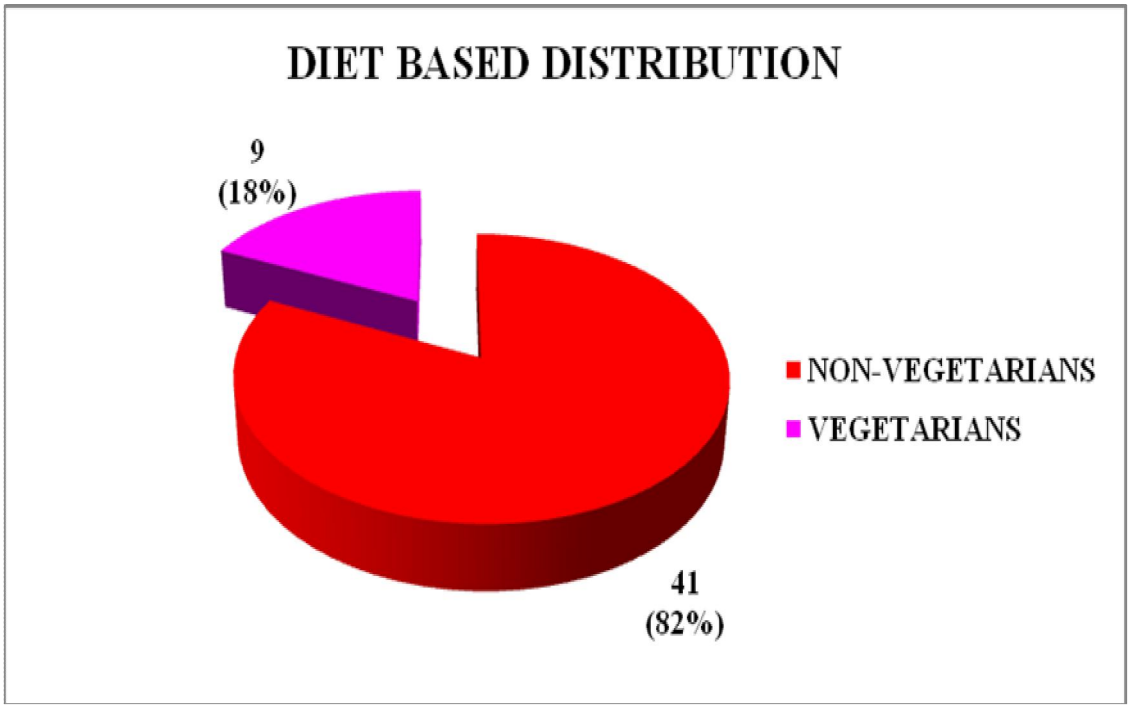


DIET BASED DISTRIBUTION

DIET PATTERN	NUMBER OF PATIENTS	PERCENTAGE
NON-VEGETARIANS	41	82%
VEGETARIANS	9	18%

41 Patients (82%) are Non-vegetarians

9 patients (18%) are Vegetarians



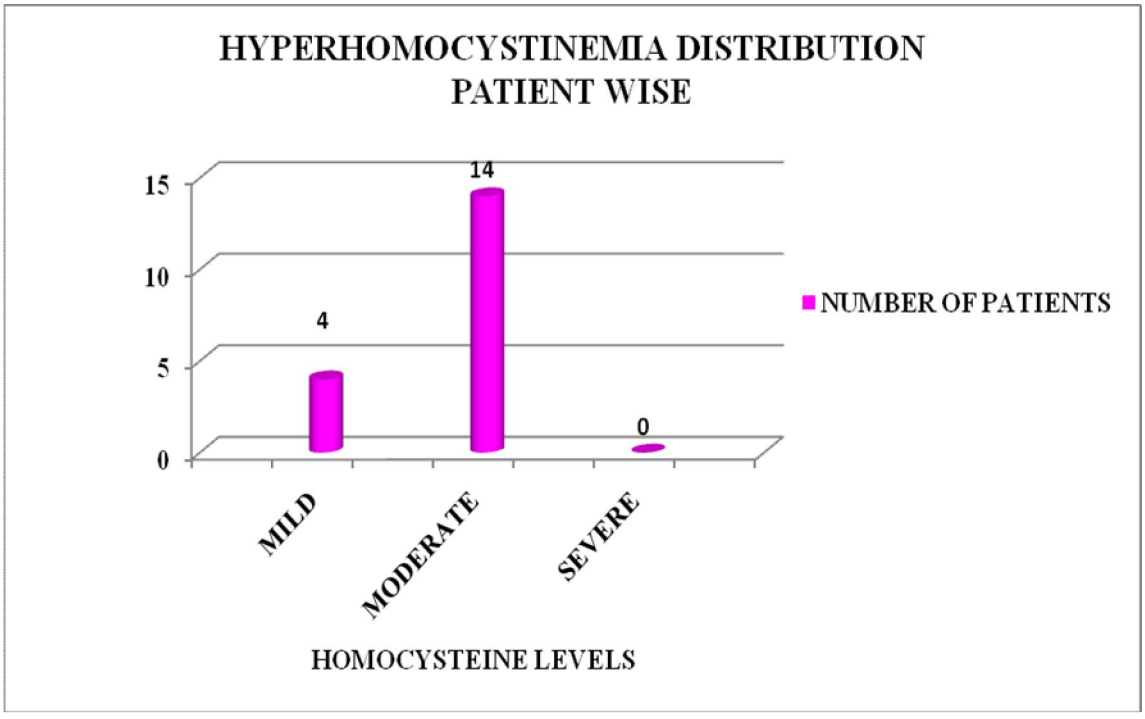
HYPERHOMOCYSTINEMIA DISTRIBUTION

PATIENT WISE

HOMOCYSTEINE LEVELS (micro mol/L)	NUMBER OF PATIENTS	PERCENTAGE
MILD (15-30)	4	22.22%
MODERATE (31-100)	14	77.77%
SEVERE (>100)	0	0%

4 Patients (22.22%) are having mild hyperhomocystinemia.

14 Patients (77.77%) are having moderate hyperhomocystinemia.



HYPERHOMOCYSTINEMIA DISTRIBUTION

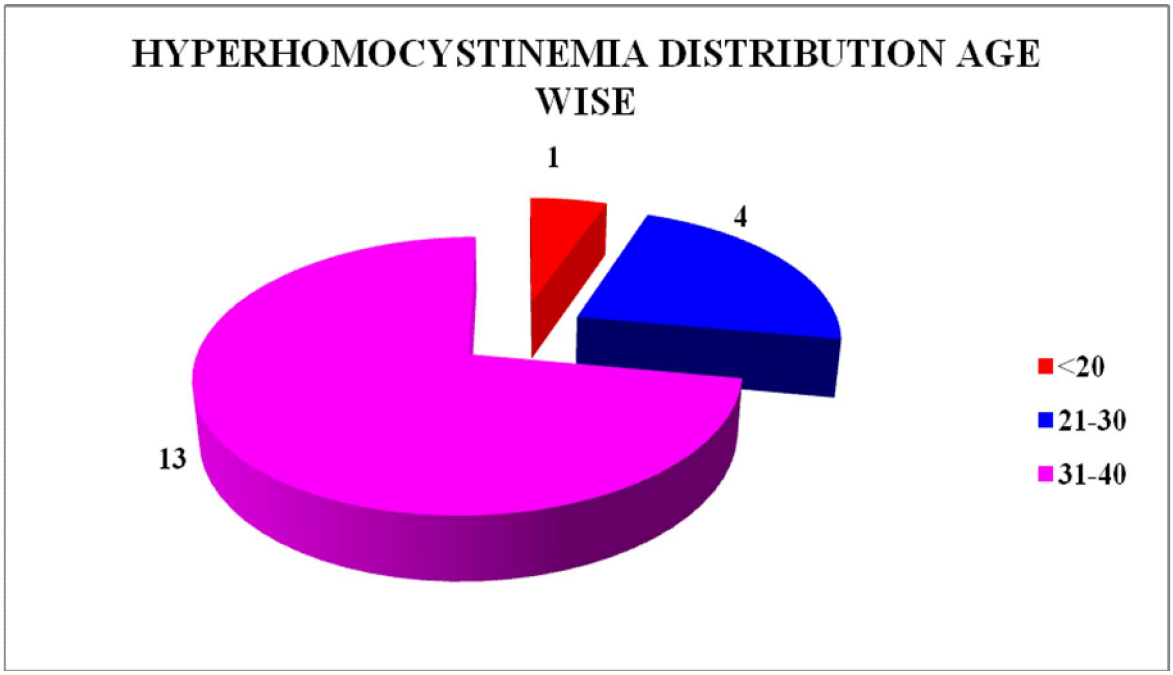
AGE WISE

AGE GROUP	NO. OF PATIENTS WITH HYPERHOMOCYSTENIMIA	PERCENTAGE
<20	1	33.33%
21-30	4	20.0%
31-40	13	48.12%

1 Patient with hyperhomocystinemia is below age 20.

4 Patients with hyperhomocystinemia are between 21 – 30.

13 Patients with hyperhomocystinemia are between 31 – 40.



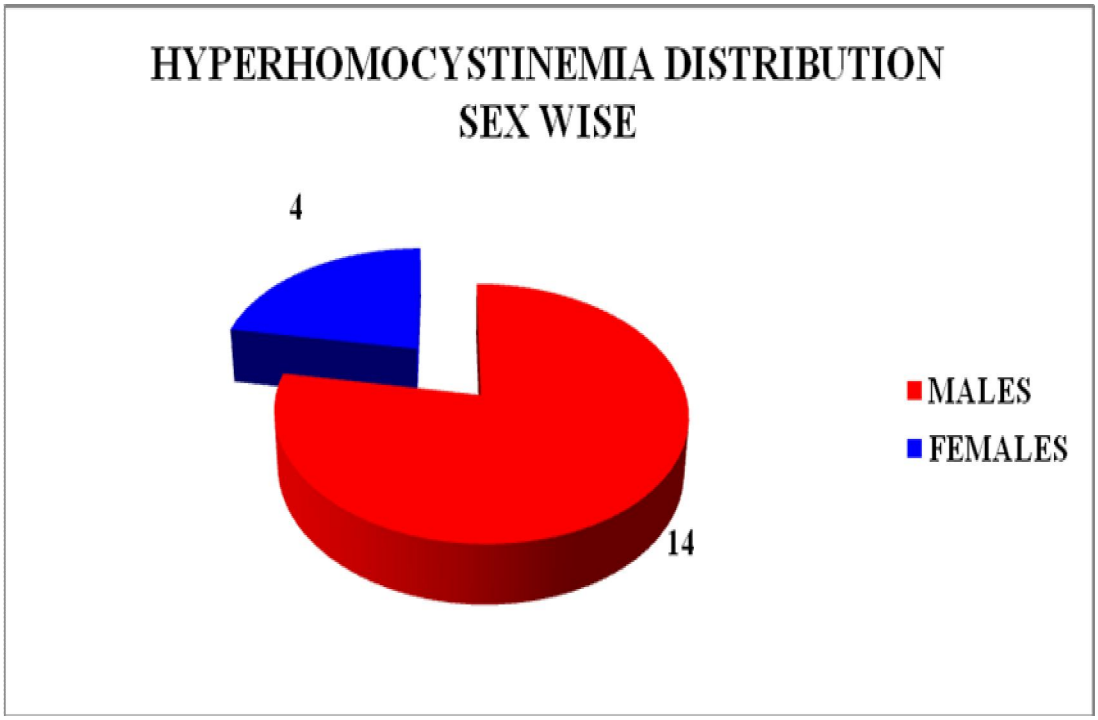
HYPERHOMOCYSTINEMIA DISTRIBUTION

SEX WISE

SEX	NUMBER OF PATIENTS WITH HYPERHOMOCYSTENIMIA	PERCENTAGE
MALES	14	33.33%
FEMALES	4	50%

14 Out of 42 males had hyperhomocystinemia

4 out of 8 females had hyperhomocystinemia

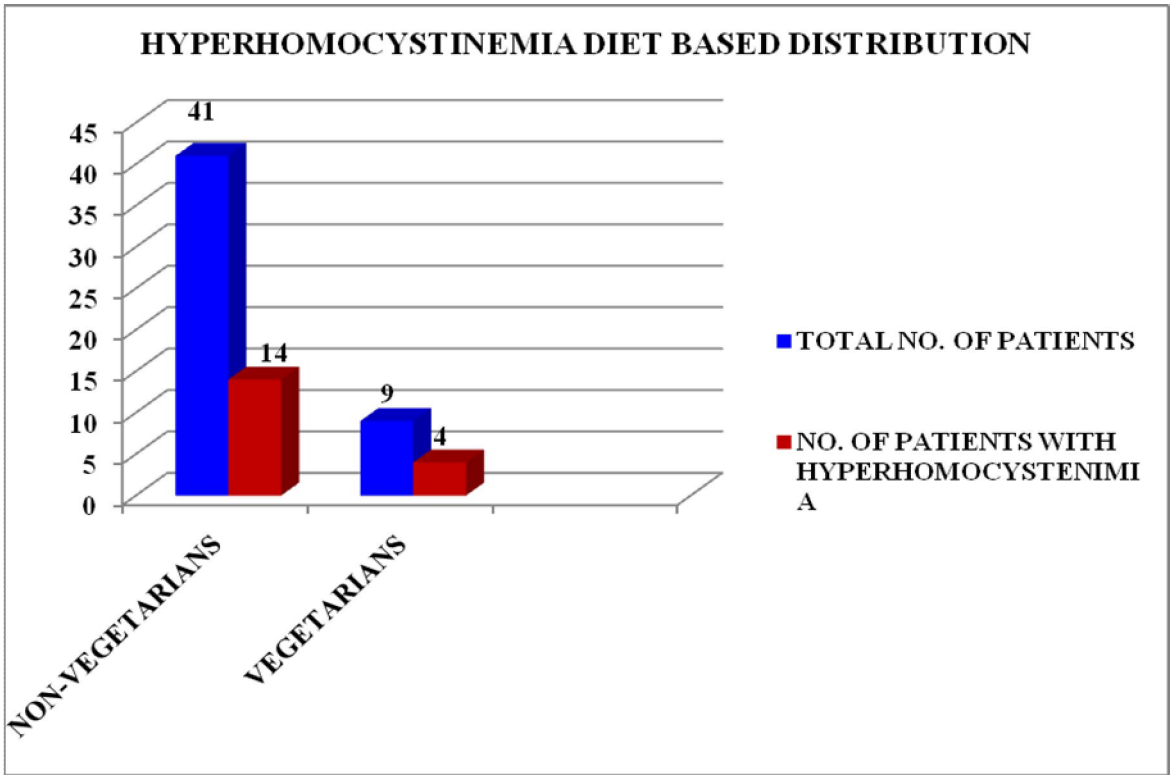


HYPERHOMOCYSTINEMIA DIET BASED DISTRIBUTION

DIET PATTERN	TOTAL NO. OF PATIENTS	NO. OF PATIENTS WITH HYPERHOMOCYSTENIMIA	PERCENTAGE
NON-VEGETARIANS	41	14	34.15%
VEGETARIANS	9	4	44.44%

14 out of 41(34.15%) non-vegetarians had hyperhomocystenimia

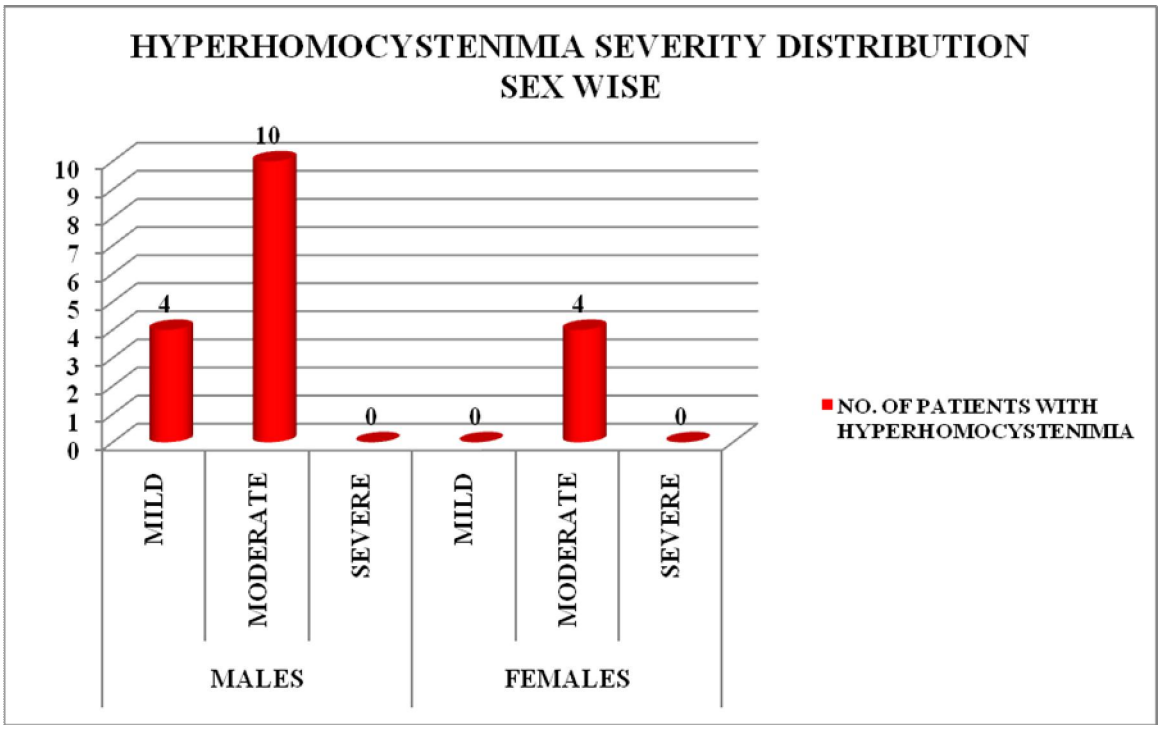
4 out of 9 (44.44%) vegetarians had hyperhomocystenimia



HYPERHOMOCYSTENIMIA SEVERITY DISTRIBUTION

SEXWISE

SEX	HYPERHOMOCYSTENIMIA SEVERITY	NO. OF PATIENTS WITH HYPERHOMOCYSTENIMIA
MALES	MILD	4
	MODERATE	10
	SEVERE	0
FEMALES	MILD	0
	MODERATE	4
	SEVERE	0

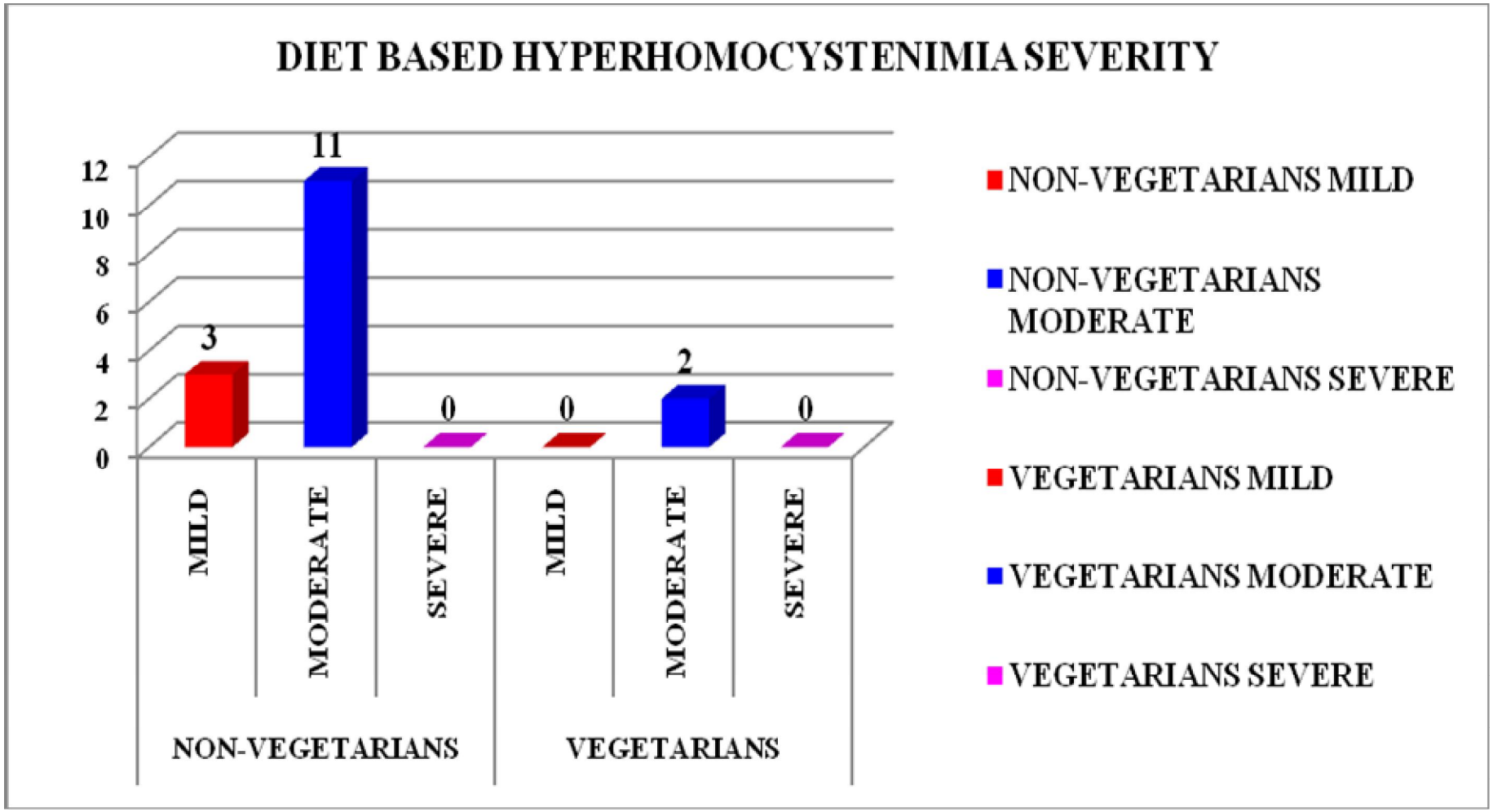


DIET BASED HYPERHOMOCYSTENIMIA SEVERITY

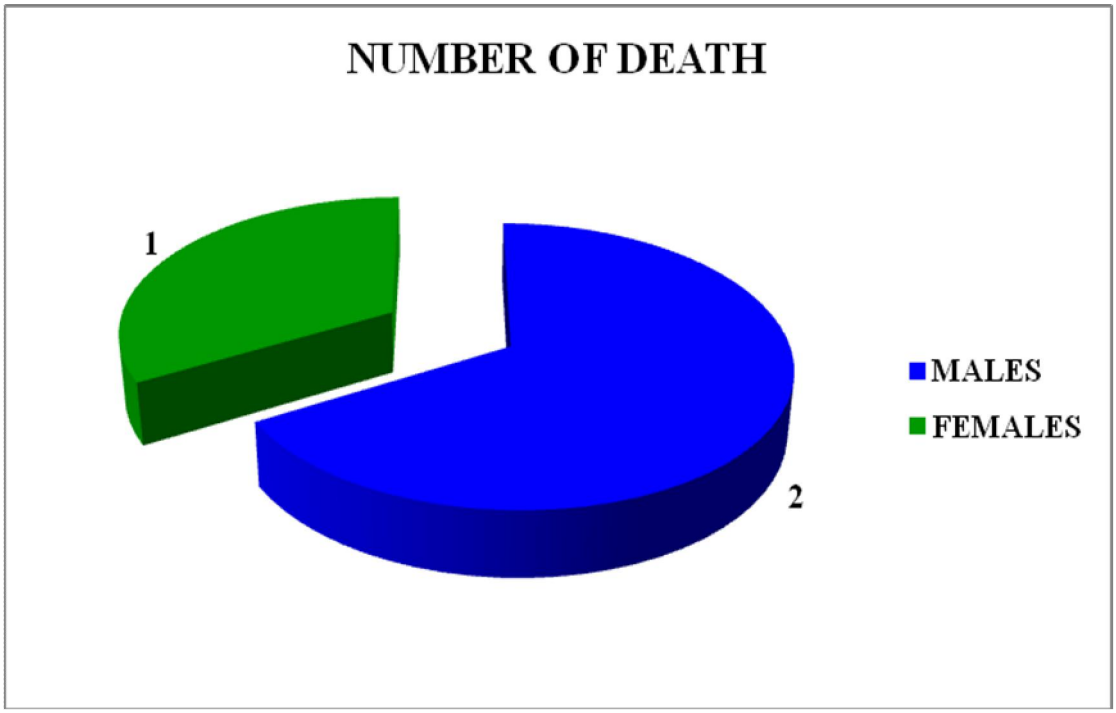
DIET PATTERN	HYPERHOMOCYSTENIMIA SEVERITY	NUMBER OF PATIENTS WITH HYPERHOMO-CYSTENIMIA
NON-VEGETARIANS	MILD	3
	MODERATE	11
	SEVERE	0
VEGETARIANS	MILD	1
	MODERATE	3
	SEVERE	0

Among non-vegetarians, 3 patients had mild hyperhomocystenimia; 11 patients had moderate hyperhomocystenimia and none had severe hyperhomocystenimia.

Among vegetarians, 1 patient had mild hyperhomocystenimia; 3 patients had moderate hyperhomocystenimia and none had severe hyperhomocystenimia.


DIET BASED HYPERHOMOCYSTENIMIA SEVERITY
12
10
8
6
4
2
0
3
11
0
0
2
0
MILD
MODERATE
SEVERE
MILD
MODERATE
SEVERE
NON-VEGETARIANS
VEGETARIANS
NON-VEGETARIANS MILD
NON-VEGETARIANS MODERATE
NON-VEGETARIANS SEVERE
VEGETARIANS MILD
VEGETARIANS MODERATE
VEGETARIANS SEVERE

SEX	NUMBER OF DEATH
MALES	2
FEMALES	1



T-Test

MALES

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
Homocysteine	**42**	**22.4826**	**23.47244**	**3.62188**

One-Sample Test

	Test Value = 15					
	t	df	Sig. (2-tailed) p value	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Homocysteine	**2.066**	**41**	**.045**	**7.4826**	**.1681**	**14.7971**

'p' value is 0.045 which is less than 0.05. Hence, this p value is statistically significant.

T-Test

FEMALES

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
Homocysteine	**8**	**30.2838**	**21.58607**	**7.63183**

One-Sample Test

	Test Value = 12					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
			p value		Lower	Upper
Homocysteine	**2.396**	**7**	**.048**	**18.2838**	**.2373**	**36.3302**

'p' value is 0.048 which is less than 0.05. Hence, this p value is statistically significant.

DISCUSSION

DISCUSSION

In our study, we took 50 patients with first attack of acute ischemic stroke between age group 12 and 40. We have excluded common conventional risk factors for stroke in young. These patients are put on all important investigations including fasting plasma homocysteine levels.

We had 42 male patients and 8 female patients with stroke. Out of them, 41 were taking non-vegetarian food substance and 9 were taking strict vegetarian food substance since their childhood period. These patients are carefully chosen as to exclude some common conditions and substances which causes significant elevation of homocysteine level. Cross sectional study was done on these patients by obtaining fasting plasma homocysteine on the second day after admission. The results are obtained after photometric analysis.

Our study shows prevalence of stroke in young is more in males when compared to females (42 patients versus 8 patients). Also the prevalence of hyperhomocystenimia is more common in males (14 patients out of 42 patients) versus females (4 patients out of 8 patients). But the proportion of hyperhomocystenimia is more in females than males (50% versus 33.33%).

Our study shows occurrence rate of stroke increases as the age increases. It is rare before age 20 (only 3 patients below age 20 had stroke). Also the prevalence of hyperhomocystenimia is more in age group between 31 – 40 (48%) as 13 out of 27 had hyperhomocystenimia.

Our study showed 14 out of 41 non-vegetarians had hyperhomocystenimia (34.15%) also 4 out of 9 vegetarians had hyperhomocystenimia (44.44%). This shows that vegetarians have higher prevalence of hyperhomocystenimia than non-vegetarians.

Our study shows most of the patients are in moderate range of hyperhomocystenimia (14 out of 18) i.e. 77.77% and none of the patients had severe hyperhomocystenimia. Five patients in our study had family history of stroke out of which 3 had hyperhomocystenimia (2 males and 1 female).

In our study, 3 out of 50 patients died in the course of treatment in the hospital during the study period. All these patients (2 males and 1 female) had hyperhomocystenimia (in moderate range).

'P' values were calculated by setting a separate cut-off values for females and males. 'P' values calculated from our study showed to be in the significant range (i.e. <0.05).

From this study, it is clearly shown that homocysteine has a definite role in stroke in young, also proportion of hyperhomocystenimia is more among vegetarians than the non-vegetarians.

CONCLUSION

CONCLUSION

1. High prevalence of elevated homocysteine in patients with stroke in young.

2. There is a definite associated of homocysteine in patients with stroke in young.

3. Homocysteine may play a role in pathogenesis as mentioned in the literature above which needs further studies.

4. Level of homocysteine has a definite role in determining the mortality in patients with stroke in young.

5. Level of homocysteine has its implication in prognosis and outcome.

SCOPE FOR FUTURE RESEARCH

Hyperhomocystenimia seems to be a risk factor for thrombotic events via its effects on platelets, vascular endothelium, and coagulation proteins. Atherogenic mechanisms promoted by homocysteine include altered Factor V formation, which catalyzes prothrombin to thrombin, decreased protein C activation, diminished fibrinolysis, and platelet aggregation. A closer look is needed at the

interaction between homocysteine and clotting factors, fibrinolytic parameters, and endothelial-derived factors.

Prospective trials utilizing treatments for lowering fibrinogen and homocysteine (e.g. fibrates and folate/B-vitamins) are needed to evaluate the merit of clinical evaluation of these variables. A reduction in risk of stroke accompanying the reduction of these concentrations must also be demonstrated before clinical determination of these values is put into practice. Several drugs have been identified which lower fibrinogen concentrations, however these drugs have additional pharmacological effects making it difficult to attribute any benefits on improving stroke risk to reduction of fibrinogen. Agents for the selective lowering of fibrinogen concentrations are under development. Treatment of homocysteinemia and its vascular complications includes folate, vitamins B12 and B6, betaine, and anticoagulants.

Higher levels of these cofactors are associated with lower concentrations of homocysteine. No information is available as to whether a reduction in homocysteine concentrations by increased intake of supplements or foods high in these vitamins reduces stroke risk.

Studies has to be done to know the exact correlation between food pattern and homocysteine levels and the role of these foods in acute vascular events.

The scientists involved in studying homocysteine are already clear danger-signal, as they have been ignored for many years while the focus was on cholesterol, and will now fight hard to maintain and improve their new status. They are already starting to make wildly exaggerated claims, such as "studies now underway will prove that controlling homocysteine is the best way to deal with vascular disease." As well as vascular disease, homocysteine is now being 'linked' with virtually every other known ailment, Alzheimer's, Bechets disease ,inflammatory bowel disease certain vasculitis ,osteoporosis and strokes. All that seems certain at the moment is that elevated homocysteine is associated with ageing, as are most of the diseases 'linked' to homocysteine.

Homocysteine is being labelled as "NEWER CHOLESTEROL" by certain epidemiologist.Still more study is required to know the exact relation of homocysteine in various diseases.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Government of India, Central Bureau of Health Intelligence, National Health Profile 2008. New Delhi: Directorate General of Health Sciences; 2008. p.102.
2. Workshop report on Stroke surveillance in India. World Health Organization. New Delhi. Available from: http://www.whoindia.org/.../NMH_Resources_cvd_MGMT_icmrSTROKE_ SURVEILLANCE.pdf. [Last cited on 2006].
3. Warlow CP, Dennis MS, Gijn van J, Hankey GJ, Sandercock PA, Bamford JM, *et al*. *Stroke A Practical guide to management.* 2nd edition. Oxford: Blackwell Sciences; 2001.
4. Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: A review of population-based studies of incidence, prevalence, and case-fatality in the late 20 th century. *Lancet Neurol* 2003;2:43-53.
5. Nayak SD, Nair M, Radhakrishnan K, Sarma PS. Ischaemic stroke in the young adult: Clinical features, risk factors and outcome. *Natl Med J India* 1997;10:107-12.
6. Lipska K, Sylaja PN, Sarma PS, Thankappan KR, Kutty VR, Vasan RS, *et al*. Risk factors for acute ischemic stroke in young adults in South India. *J Neurol Neurosurg Psychiatry* 2007;78:959-63.
7. Razdan S, Koul RL, Motta A, Kaul S. Cerebrovascular disease in rural Kashmir, India. *Stroke* 1989;20:1691-3.
8. Abraham J, Rao PS, Inbaraj SG, Shetty G, Jose CJ. An epidemiological study of hemiplegia due to stroke in South India. *Stroke* 1970;1:477-81
9. Das SK, Banerjee TK, Biswas A, Roy T, Raut DK, Mukherjee CS, *et al*. A prospective community-based study of stroke in Kolkata, India. *Stroke* 2007;38:906-10

10. Dalal PM, Malik S, Bhattacharjee M, Trivedi ND, Vairale J, Bhat P, *et al*. Population-based stroke survey in Mumbai, India: Incidence and 28-day case fatality. *Neuroepidemiology* 2008;31:254-61.

11. Adams HP Jr, Kappelle LJ, Biller J, Gordon DL, Love BB, Gomez F, *et al*. Ischemic stroke in young adults. Experience in 329 patients enrolled in the Iowa Registry of stroke in young adults. *Arch Neurol* 1995;52:491-5.

12. Kittner SJ, Stern BJ, Wozniak M, Buchholz DW, Earley CJ, Feeser BR, *et al*. Cerebral infarction in young adults: The Baltimore-Washington Cooperative Young Stroke Study. *Neurology* 1998;50:890-4.

13. You RX, McNeil JJ, O′Malley HM, Davis SM, Thrift AG, Donnan GA. Risk factors for stroke due to cerebral infarction in young adults. *Stroke* 1997;28:1913-8.

14. Marini C, Totaro R, De Santis F, Ciancarelli I, Baldassarre M, Carolei A. Stroke in young adults in the community-based L′Aquila registry: Incidence and prognosis. *Stroke* 2001;32:52-60.

15. Jacobs BS, Boden-Albala B, Lin IF, Sacco RL. Stroke in the young in the northern Manhattan stroke study. *Stroke* 2002;33:2789-93.

16. Lee TH, Hsu WC, Chen CJ, Chen ST. Etiologic study of young ischemic stroke in Taiwan. *Stroke* 2002;33:1950-5.

17. Leys D, Bandu L, Hınon H, Lucas C, Mounier-Vehier F, Rondepierre P, *et al*. Clinical outcome in 287 consecutive young adults (15 to 45 years) with ischemic stroke. *Neurology* 2002;59:26-33.

18. Kristensen B, Malm J, Carlberg B, Stegmayr B, Backman C, Fagerlund M, *et al*. Epidemiology and etiology of ischemic stroke in young adults aged 18 to 44 years in northern Sweden. *Stroke* 1997;28:1702-9.

19. Nedeltchev K, der Maur TA, Georgiadis D, Arnold M, Caso V, Mattle HP, *et al*. Ischemic stroke in young adults: Predictors of outcome and recurrence. *J Neurol Neurosurg Psychiatry* 2005;76:191-5.

20. Putaala J, Metso AJ, Metso TM, Konkola N, Kraemer Y, Haapaniemi E, *et al*. Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: The Helsinki young stroke registry. *Stroke* 2009;40:1195-203.

21. Verona JF, Bermejo F, Guerra JM, Molina JA. Long-term prognosis of ischemic stroke in young adults: Study of 272 cases. *J Neurol* 2004;251: 1507-14.

22. Prasad K. Stroke in young. *Natl Med J India* 1997;10:103-4.

23. Sridharan R. Risk factors for ischemic stroke: A case control analysis. *Neuroepidemiology* 1992;11:24-30.

24. Gunarathne A, Patel JV, Potluri R, Gammon B, Jessani S, Hughes EA, *et al*. Increased 5-year mortality in the migrant South Asian stroke patients with diabetes mellitus in the United Kingdom: The West Birmingham Stroke Project. *Int J Clin Pract* 2008;62:197-201.

25. Bansal BC, Prakash C, Jain AL, Brahmanandan KR. Cerebrovascular disease in young individuals below the age of 40 years. *Neurol India* 1973;21:11-8.

26. Chopra JS, Prabhakar S. Clinical features and risk factors in stroke in young. *Acta Neurol Scand* 1979;60:289-300.

27. Dalal PM. Stroke in thyoung in West-Central India. Vol. 25. Advances in neurology. In: Goldstein, Bolis L, Fieschi C, Gorini S, Millikan CG, editors. New York: Raven Press; 1979. p. 339-48.

28. Radhakrishnan K, Ashok PP, Sridharan R, Mousa ME. Stroke in the young: Incidence and pattern in Benghazi, Libya. *Acta Neurol Scand* 1986;73: 434-8.

29. Bogousslavsky J, Regli FF. Ischemic stroke in adults younger than 30 years of age: Cause and prognosis. *Arch Neurol* 1987;44:479-82.

30. Chancellor AM, Glasgow GL, Ockelford PA, Johns A, Smith J. Etiology, prognosis, and hemostatic function after cerebral infarction in young adults. *Stroke* 1989;20:477-82.

31. Lanzino G, Andreoli A, Di Pasquale G, Urbinati S, Limoni P, Serracchioli A, *et al*. Etiopathogenesis and prognosis of cerebral ischemia in young adults: A survey of 155 treated patients. *Acta Neurol Scand* 1991;84:321-5.

32. Lisovoski F, Rousseaux P. Cerebral infarction in young people: A study of 148 patients with early cerebral angiography. *J Neurol Neurosurg Psychiatry* 1991;54:576-9.

33. Leno C, Berciano J, Combarros O, Polo JM, Pascaul J, Quinatana F, *et al*. A prospective study of stroke in young adults in Cantabria, Spain. *Stroke* 1993;24:792-5.

34. Luthra K, Prasad K, Kumar P, Dwivedi M, Pandey RM, Das N. Apolipoprotein E gene polymorphism in cerebrovascular disease: A case-control study. *Clin Genet* 2002;62:39-44.

35. Munshi A, Sultana S, Kaul S, Reddy BP, Alladi S, Jyothy A. Angiotensin-converting enzyme insertion/deletion polymorphism and the risk of ischemic stroke in a South Indian population. *J Neurol Sci* 2008;272:132-5.

36. Alluri RV, Mohan V, Komandur S, Chawda K, Chaudhuri JR, Hasan Q. MTHFR C677T gene mutation as a risk factor for arterial stroke: A hospital based study. *Eur J Neurol* 2005;12:40-4.

37. Gretarsdottir S, Thorleifsson G, Reynisdottir ST, Manolescu A, Jonsdottir S, Jonsdottir T, *et al*. The gene encoding phosphodiesterase 4D confers risk of ischemic stroke. *Nat Genet* 2003;35:131-8.

38. Munshi A, Babu MS, Kaul S, Shafi G, Anila AN, Alladi S, *et al*. Phosphodiesterase 4D (PDE4D) gene variants and the risk of ischemic stroke in a South Indian population. *J Neurol Sci* 2009;285:142-5.

39. Munshi A, Aliya N, Jyothy A, Kaul S, Alladi S, Shafi G. Prothrombin gene G20210A mutation is not a risk factor for ischemic stroke in a South Indian Hyderabadi Population. Thromb Res 2009;124:245-7.

40. Prasad K, Kaul S, Padma MV, Gorthi SP, Khurana D, Bakshi A. National Guidelines for Management of Stroke in India. First edition. New Delhi. India. Indian Academy of Neurology and Indian Stroke Association, Working Committee for stroke Guidelines. 2010.

41. Bousser MG, Ferro JM. Cerebral venous thrombosis: An update. *Lancet* Neurol 2007;6:162-70.

42. Assadian A, Senekowitsch C, Rotter R, Zφlss C, Strassegger J, Hagmóller GW. Long-term results of covered stent repair of internal carotid artery dissections. *J Vasc Surg* 2004;40:484-7.

43. World Health Organisation, World Health Statistics Quarterly 1993; 46; 1 – 2.

44. World Health Organization, World Health Statistics Quarterly 1995; 48; 3 – 4 .

45. Dubey G.P., Sharma K. Incidence of ischaemic heart disease in urbanized community of Northern India. *QJ Surgical Sci* 1977; 13: 3 – 4.

46. Tucker K.L., Selhub J., Wilson P.W., Rosenberg I.H. Dietary intake pattern relates to plasmafolate and homocysteine concentration in the Framingham Heart Study. *J Nutr* 1996; 126: 3025 – 31.

47. Vermaak W.J., Ubbink J.B., Pelport R et al. Ethinic immunity to coronary heart disease? *Atherosclerosis* 1991; 89: 155 – 62.

48. Cravo M.L., Gloria L.M., Selhub J et al. Hyperhomocysterosis in chronic alcoholism. Correlation with folate, vitamin B-12 and vitamin B-6 status. *Am J Clin Nutr* 1996; 63: 220 – 24.

49. Lussier-Cacan S., Xhignesse M., Piolot A et al. Plasma total homocysteine in healthy subjects – sex-specific relation with biological traits. *Am J Clin Nutr* 1996; 64: 587 – 93.

50. Kang S.S., Wrong P.W.K., Malinow M.R. Hyperhomocysterinaemia as a risk factor for occlusive vascular disease. *Ann Rev Nutr* 1992; 12: 27 – 98.

51. Graham I.M., Daly L.E., Refgum H.M., et al. Plasma homocysteine as a risk factor for occlusive vascular disease. The European concerted action project. *JAMA* 1997; 277: 1775 – 81.

52. Boushey C.J., Beresfod S.A., Omen G.S., Motulsky A.G. A Quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits in-creasing folic acid intakes. *JAMA* 1995; 274: 1049 – 57.

53. Knekt P., Alftnan G., Aromaa A. et al. Homocysteine and major coronary events: a prospective population study amongst women. *J Intern Med* 2001; 249: 461 – 5.

54. Yeolekar ME, Shete MM. Homocysteine and Hypertension. *JAPI* 2002; 50: 29 – 35.

55. Wu K.K., Thiagarajan P. Role of endothelium in thrombosis and haemostasis. *Annu Rev Med* 1996; 47: 315 – 31.

56. Alftman G., Pekkanen J., Jauhiainen M., et al. Relation of serum homocysteine and lipoprotein (a) concentration to atherosclerotic disease in a prospective finish population based study. Arthrosclerosis 1994; 106: 9 – 19.

57. Evans R.W., Shaten B.J., Hempel J.D. et al. Homocysteine and risk of cardiovascular disease in the multiple risk factor intervention trial. *Artherioscler Thromb Vasc Biol* 1997; 17: 1947 – 53.

58. Folsom A.E., Neito F.J., McGoern P.G. et al. Prospective study of coronary heart disease incidence in relation to fasting total homocysteine, related genetic polymorphism and B vitamins: the atherosclerosis risk in communities (ARIC) study. *Circulation* 1998; 98: 204 – 10.

59. Dudman N.P.B. An alternative view of homocysteine. *Lancet* 1999; 354: 2072 – 4.

60. Chambers JC, Obied OA, Refsum H. et al. Plasma homocysteine concentrations and risk of coronary heart disease in UK Indian Asian and European men. *Lancet* 200; 355: 523 – 7.

61. Deepa R, Velmurugan K, Saravanan G, Karkuzhali K, Swarakanath V, Mohan V. Absence of association between serum homocysteine levels and coronary artery disease in South Indian males. *Indian Heart J* 2001; 53: 44 – 7.

62. Anand SS, Yusuf S, Vuksan V. et al. Differences in risk factors, atherosclerosis and cardiovascular disease between ethnic groups in Canada; the study of health assessment and risk ethnic groups (SHARE). *Indian Heart J* 2000; 52(7 Suppl): 535 – 43.

63. Anand SS, Yusuf S, Vuksan V. et al. Differences in risk factors, atherosclerosis and cardiovascular disease between ethnic groups in Canada; the study of health assessment and risk ethnic groups (SHARE). *Indian Heart J* 2000; 356: 279 – 84.

64. Chambers JC, Obeid OA, Refsum H. et al. Plasma homocysteine concentrations and risk of coronary heart disease in UK Indian Asian and European men. *Lancet* 2000: 355(9203): 523 – 7.

65. Mendis S., Athuda S.B., Naser M. et al. Association between hyperhomocysteinaemia and hypertension in Sri Lankans. *J Int Med* 1999; 27: 138 – 44.

66. Bortolotto L.A., Safar M.E., Billaud E. Plasma homocysteine, aortic stiffness and renal function in hypertensive patients. *Hypertension* 1999; 34: 837 – 42.

67. Adunsky A., Witzman A., Fleissing Y et al. The relation of plasma total homocysteine levels to prevalent cardiovascular disease in older patients with ischaemic stroke. *Aging* 2000; 12: 48 – 52.

68. Cheng S.W., Ting A.C., Wong J. Fasting total plasma homocysteine and atherosclerotic peripheral vascular disease. *Ann Vasc Surg* 1997; 11: 217 – 23.

69. Den Heiser M., Koster T., Blom H.J. et al. Hyperhomocysteinaemia as a risk factor for deep vein thrombosis. *N Eng J Med* 1996; 334: 759 – 62.

70. Francesco P. Cappuccio, Rachel Bell, Ivan J. Perry, Julie Gilg, Per M.Ueland Helga Refsum, Giuseppe A. Sagnella, Steve Jeffery, Derek G. Cook. Homocysteine levels in men and women of different ethnic and cultural background living in England. *Atherosclerosis* 164 (2002) 95 – 102.

71. Govindaiah Vinukonda. Plasma Homocysteine and Methylenetetrahydrofolate Reductase Gene Polymorphism in Human Health and Disease: An Update. *Int J Hum Genet*, 8(1-2): 171-179 (2008).

72. M. Krajčovičová-Kudláčková, P. Blažíček, J. Kopčová, A. Béderová, K. Babinská. Homocysteine Levels in Vegetarians versus Omnivores. *Annals of Nutrition & Metabolism* 2000;44:135-138

73. Francesco Parisi, Hélène Danesi, Vincenzo Di Ciommo, Francesca Fina, Germana Giannone, Franco Colistro, Roberto M. Di Donato, Glauco Catena. Treatment of hyperhomocystenimia in paediatric heart transplant recipients. *The Journal of Heart and Lung Transplantation*, Volume 22, Issue 7, July 2003, Pages 778-783.

ANNEXURE

- **PROFORMA**
- **MASTER CHART**
- **ABBREVIATIONS**
- **ETHICAL COMMITTEE APPROVAL ORDER**

PROFORMA

Name Sex Age

Religion Address

Citizenship

Complaints:

Past H/o:

Similar episodes Bronchial Asthma

Transient Ischemic Attack Tuberculosis

Diabetes Mellitus Human immunodeficiency virus

Hypertension Drug Allergy

Coronary Artery Disease Others

Personal H/o:

Diet (Vegetarian/Non.Vegetarian)

Marital status Premarital / Extra marital sexual history

Mensural H/o

Habits: Alcohol Tobacco chewing

Smoking Betel Nut chewing

Family H/o:

Treatment H/o:

GENERAL EXAMINATION:

VITALS **Peripheral Pulses**

HEAD TO FOOT EXAMINATION

SYSTEMIC EXAMINATION

CVS

RS

Abdomen

Central Nervous system Examination

PROVISIONAL DIAGNOSIS

Sl.No	Name	Age	Sex	Diet pattern	Family H/O	Blood Pressure	Fasting Blood Sugar <120mg%	Total Carbohydrate <200 mg%	Triglyceride <150 mg%	Low Density Lipoprotein <100 mg%	High Density Lipoprotein <50 mg% – Female <40 mg% - Male	Thyroid Stimulating Hormone in normal limits	Echocardiography	CT Brain	4 vessel Doppler	Homocysteine Levels in Micromole/L Male 5 – 15; female 3 – 12
1	PRASANTH	33	M	Non-Vegetarian	No	160/90	Yes	No	No	No	No	Yes	No	R /MCA	Nil	29.31
2	SARAVANAN	28	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	L/PCA	Nil	36.48
3	SELVAM	30	M	Non-Vegetarian	No	120/80	Yes	No	No	No	No	Yes	No	L /MCA	Nil	10.52
4	JOHN	37	M	Non-Vegetarian	No	130/80	Yes	No	No	No	No	Yes	No	R /MCA	Nil	9.22
5	MANI	28	M	Non-Vegetarian	No	134/80	Yes	No	No	No	No	Yes	No	R /MCA	Nil	24.32
6	ELANGOVAN	38	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	MVP	L/PCA	Nil	5.48
7	DEVI	25	F	Non-Vegetarian	No	130/80	Yes	No	No	No	No	Yes	No	L /MCA	Nil	52.42
8	ARUNAGIRI	35	M	Vegetarian	No	160/80	Yes	No	No	No	No	Yes	No	R /MCA	Nil	20.66
9	AMUDHA	27	F	Non-Vegetarian	Yes	140/80	Yes	No	No	No	No	Yes	No	R/ACA	Nil	10.94
10	HABEEB	36	M	Non-Vegetarian	No	140/84	Yes	No	No	No	No	Yes	No	L/PCA	Nil	68.28
11	RANGASWAMY	39	M	Vegetarian	No	No	Yes	No	No	No	No	Yes	No	R /MCA	Nil	12.38
12	CHRISTOPHER	34	M	Non-Vegetarian	No	150/80	Yes	No	No	No	No	Yes	No	L /MCA	Nil	80.28
13	THULASI	28	F	Non-Vegetarian	No	140/90	Yes	No	No	No	No	Yes	PFO	R /MCA	Nil	9.45
14	MARIMUTHU	38	M	Non-Vegetarian	No	140/86	Yes	No	No	No	No	Yes	No	R /MCA	RCS	30.68

Sl.No	Name	Age	Sex	Diet pattern	Family H/O	Blood Pressure	Fasting Blood Sugar <120mg%	Total Carbohydrate <200 mg%	Triglyceride <150 mg%	Low Density Lipoprotein <100 mg%	High Density Lipoprotein <50 mg% – Female <40 mg% - Male	Thyroid Stimulating Hormone in normal limits	Echocardiography	CT Brain	4 vessel Doppler	Homocysteine Levels in Micromole/L Male 5 – 15; female 3 – 12
15	RANI	22	F	Vegetarian	No	130/90	Yes	No	No	No	No	Yes	No	R/PCA	Nil	10.24
16	NAVEEN	27	M	Non-Vegetarian	No	140/90	Yes	No	No	No	No	Yes	No	R/ACA	Nil	12.38
17	VENKATESH	30	M	Vegetarian	No	150/84	Yes	No	No	No	No	Yes	No	L /MCA	Nil	6.68
18	RAJALAXMI	29	F	Non-Vegetarian	No	130/90	Yes	No	No	No	No	Yes	No	L /MCA	Nil	10.48
19	ABDULLA	37	M	Non-Vegetarian	Yes	130/80	Yes	No	No	No	No	Yes	No	R /MCA	Nil	10.58
20	MURUGAN	18	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	R /MCA	Nil	8.28
21	GUGAN	27	M	Non-Vegetarian	No	130/80	Yes	No	No	No	No	Yes	No	R /PCA	Nil	7.56
22	BALAJI	35	M	Non-Vegetarian	No	140/80	Yes	No	No	No	No	Yes	No	R /MCA	Nil	8.92
23	SIVA	33	M	Non-Vegetarian	No	126/80	Yes	No	No	No	No	Yes	No	L /MCA	Nil	10.37
24	ASLAM	24	M	Non-Vegetarian	Yes	179/100	Yes	No	No	No	No	Yes	MVP	L/PCA	Nil	68.48
25	ARUMUGAM	35	M	Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	R/MCA	Nil	7.76
26	RAMESH	26	M	Non-Vegetarian	No	120/80	Yes	No	No	No	No	Yes	No	R/PCA	Nil	8.82
27	PETER	36	M	Non-Vegetarian	No	130/80	Yes	No	No	No	No	Yes	No	L/MCA	Nil	20.38
28	ARUN	39	M	Non-Vegetarian	No	160/90	Yes	No	No	No	No	Yes	No	L/PCA	Nil	90.62

Sl.No	Name	Age	Sex	Diet pattern	Family H/O	Blood Pressure	Fasting Blood Sugar <120mg%	Total Carbohydrate <200 mg%	Triglyceride <150 mg%	Low Density Lipoprotein <100 mg%	High Density Lipoprotein <50 mg% – Female <40 mg% - Male	Thyroid Stimulating Hormone in normal limits	Echocardiography	CT Brain	4 vessel Doppler	Homocysteine Levels in Micromole/L Male 5 – 15; female 3 – 12
29	SUSHEELA	38	F	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	L/MCA	Nil	45.26
30	SHANKAR	18	M	Non-Vegetarian	No	140/90	Yes	No	No	No	No	Yes	Pfo	R/MCA	Nil	10.56
31	VELU	32	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	R/MCA	RCS	40.68
32	RAMADOSS	27	M	Vegetarian	No	150/80	Yes	No	No	No	No	Yes	No	L/MCA	Nil	12.38
33	POOGODI	32	F	Non-Vegetarian	Yes	140/90	Yes	No	No	No	No	Yes	MVPS	R/MCA	Nil	55.24
34	RAHUMAN	38	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	R/MCA	Nil	12.38
35	DHARMAN	39	M	Non-Vegetarian	No	140/90	Yes	No	No	No	No	Yes	No	L/MCA	Nil	8.22
36	KUMARAN	26	M	Non-Vegetarian	No	160/80	Yes	No	No	No	No	Yes	No	R/MCA	Nil	7.36
37	RAJARAJAN	36	M	Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	R/ACA	Nil	40.72
38	ALAGAPAN	34	M	Non-Vegetarian	No	140/90	Yes	No	No	No	No	Yes	No	L/MCA	Nil	12.38
39	RAJENDRAN	36	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	R/MCA	Nil	11.38
40	SENTHILKUMAR	28	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	L/MCA	Nil	10.38
41	MANOHARAN	36	M	Non-Vegetarian	No	150/90	Yes	No	No	No	No	Yes	No	R/MCA	Nil	30.58
42	VEERASWAMY	28	M	Non-Vegetarian	No	140/86	Yes	No	No	No	No	Yes	No	L/MCA	Nil	7.72

Sl.No	Name	Age	Sex	Diet pattern	Family H/O	Blood Pressure	Fasting Blood Sugar <120mg%	Total Carbohydrate <200 mg%	Triglyceride <150 mg%	Low Density Lipoprotein <100 mg%	High Density Lipoprotein <50 mg% – Female <40 mg% - Male	Thyroid Stimulating Hormone in normal limits	Echocardiography	CT Brain	4 vessel Doppler	Homocysteine Levels in Micromole/L Male 5 – 15; female 3 – 12
43	MOHAMAD RAFIK	38	M	Non-vegetarian	No	150/86	Yes	No	No	No	No	Yes	No	L/MCA	Nil	11.28
44	PUNITHA	18	F	Vegetarian	No	160/90	Yes	No	No	No	No	Yes	No	R/MCA	Nil	48.24
45	YOGESHWARAN	26	M	Non-Vegetarian	Yes	150/90	Yes	No	No	No	No	Yes	No	L/MCA	Nil	12.28
46	VISHNU	32	M	Non-Vegetarian	No	160/90	Yes	No	No	No	No	Yes	No	R/MCA	Nil	8.23
47	SHANKAR	35	M	Non-Vegetarian	No	120/80	Yes	No	No	No	No	Yes	No	R/MCA	Nil	9.62
48	DHINAKARAN	35	M	Vegetarian	Yes	160/90	Yes	No	No	No	No	Yes	No	R/PCA	Nil	90.78
49	JOSEPH	28	M	Non-Vegetarian	No	150/88	Yes	No	No	No	No	Yes	No	R/MCA	Nil	8.28
50	ESHWARAN	26	M	Non-Vegetarian	No	120/80	Yes	No	No	No	No	Yes	No	L/PCA	Nil	10.36

ABBREVIATIONS

CVA	**:**	**CEREBRO VASCULAR ACCIDENT**
CVD	**:**	**CARDIO VASCULAR DISEASE**
Hcy	**:**	**HOMOCYSTEINE**
R	**:**	**RIGHT**
L	**:**	**LEFT**
MCA	**:**	**MIDDLE CEREBRAL ARTERY**
ACA	**:**	**ANTERIOR CEREBRAL ARTERY**
PCA	**:**	**POSTERIOR CEREBRAL ARTERY**
RCS	**:**	**RIGHT CAROTID (INTERNAL) STENOSIS**
LCS	**:**	**LEFT CAROTID (INTERNAL) STENOSIS**
MVP	**:**	**MITRAL VALVE PROLAPSE**
PFO	**:**	**PATENT FORAMEN OVULE**
SLE	**:**	**SYSTEMIC LUPUS ERYTHAMATOSIS**
RA	**:**	**RHEUMATOID ARTHRITIS**

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INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-600 003

Telephone 25363970
Fax 044 2535115
Dated : 12.05.2010

L.Dis.No.14597/ME5/Ethics Dean/MMC/2010

Title of the work : "Prevalence of Elevated Homocystaine level in patients with Stroke in Young."

Principal Investigator : Dr. R. Vivek Praveen
Designation : PG in MD General Medicine
Department :

Madras Medical College & GGH, Ch-3.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 12th May 2010 at 2.p.m in Pharmacology Seminar Hall, Madras Medical College, Chennai -3

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
4. You should not deviate form the area of the work for which you applied for ethical clearance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulation of the institution(s).
7. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, MMC,CHENNAI

CHAIRMAN
IEC,MMC, CHENNAI

DEAN
MADRAS MEDICAL COLLEGE,
CHENNAI -3